A RANDOMIZED TRIAL OF INTRAVENOUS LABETALOL VERSUS ORAL NIFEDIPINE IN ACUTE BLOOD PRESSURE CONTROL IN HYPERTENSIVE EMERGENCIES OF PREGNANCY

Dissertation submitted to

The Tamilnadu Dr. M. G. R. Medical University

in partial fulfilment of the regulations for the award of the degree of

M. S. – BRANCH II

OBSTETRICS AND GYNAECOLOGY

K. A. P. Viswanatham Government Medical College

Tiruchirapalli

The Tamilnadu Dr. M. G. R. Medical University

Chennai

April 2014

CERTIFICATE

This is to certify that the dissertation titled **'A RANDOMIZED TRIAL OF INTRAVENOUS LABETALOL VERSUS ORAL NIFEDIPINE IN ACUTE BLOOD PRESSURE CONTROL IN HYPERTENSIVE EMERGENCIES OF PREGNANCY'** is a bonafide work done by **Dr. V. B. MADHANGI** at **K. A. P. Viswanatham Government Medical College, Trichy**. This dissertation is submitted to Tamilnadu Dr. M. G. R. Medical University in partial fulfilment of university rules and regulations for the award of M. S. Degree in Obstetrics and Gynaecology.

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DECLARATION

I, **Dr. V. B. MADHANGI**, solemnly declare that the dissertation titled **'A RANDOMIZED TRIAL OF INTRAVENOUS LABETALOL VERSUS ORAL NIFEDIPINE IN ACUTE BLOOD PRESSURE CONTROL IN HYPERTENSIVE EMERGENCIES OF PREGNANCY'** is a bonafide work done by me at **K. A. P. Viswanatham Government Medical College, Trichy,** during the years 2012 to 2013 under the guidance and supervision of **Prof. Dr. D. PARIMALA DEVI, M.D., D.G.O.**, Professor and Head of the department of Obstetrics and Gynaecology. This dissertation is submitted to Tamilnadu Dr. M. G. R. Medical University in partial fulfilment of university rules and regulations for the award of M. S. Degree (Branch - II) in Obstetrics and Gynaecology.

Place

Date Dr. V. B. Madhangi

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A RANDOMIZED TRIAL OF INTRAVENOUS LABETALOL VERSUS ORAL NIFEDIPINE IN ACUTE BLOOD PRESSURE CONTROL IN HYPERTENSIVE EMERGENCIES OF PREGNANCY

ABSTRACT

OBJECTIVE: To compare safety and efficacy of intravenous labetalol with oral nifedipine to control blood pressure in hypertensive emergencies of pregnancy.

DESIGN: A prospective randomized double blind comparative clinical trial

SETTING: Patients admitted to Mahatma Gandhi Memorial government hospital, Tiruchirapalli.

POPULATION: All pregnant women with sustained severe hypertension.

METHODS: 106 consecutive patients were randomized to receive either intravenous labetalol in escalating doses of 20 mg, 40 mg, 80 mg, 80 mg, and 80 mg along with placebo tablets or nifedipine 10 mg tablet orally along with placebo saline injections every 15 minutes up to five doses. The treatment is crossed over to the other group if reduction in both systolic and diastolic blood pressure ≤ 150/100 mm Hg does not occur.

PRIMARY OUTCOME: The time taken to achieve a target blood pressure of both ≤ 150 mm Hg systolic and ≤ 100 mm Hg diastolic blood pressure.

RESULTS: The median time take taken to attain target blood pressure was 45 minutes and 30 minutes in labetalol and nifedipine groups, respectively (P = 0.17). Median number of doses required was three and two to achieve blood pressure control in labetalol and nifedipine groups, respectively (P = 0.23). Cross over treatment was required in 9.40% in labetalol group and 11.30% in nifedipine group (P = 0.75). Side effects profile between the two drugs were also similar (P = 0.06)

CONCLUSIONS: Intravenous labetalol and oral nifedipine are equally efficacious in controlling hypertensive emergencies of pregnancy.

KEYWORDS: Preeclampsia, eclampsia, labetalol, nifedipine, sustained severe hypertension

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A RANDOMIZED TRIAL OF INTRAVENOUS LABETALOL VERSUS ORAL NIFEDIPINE IN ACUTE BLOOD PRESSURE CONTROL IN HYPERTENSIVE EMERGENCIES OF PREGNANCY Dissertation submitted to The Tamilnadu Dr. M. G. R. Medical University in partial fulfilment of the regulations for the award of the degree of M. D. – BRANCH II OBSTETRICS AND GYNAECOLOGY K. A. P. Viswanatham Government Medical College Tiruchirapalli The Tamilnadu Dr. M. G. R. Medical University Chennai April 2014 CERTIFICATE This is to certify that the dissertation titled 'A RANDOMIZED TRIAL OF INTRAVENOUS LABETALOL VERSUS ORAL NIFEDIPINE IN ACUTE BLOOD PRESSURE CONTROL IN HYPERTENSIVE EMERGENCIES OF PREGNANCY' is a bonafide work done by Dr. V. B....

CONTENTS

INTRODUCTION

Hypertension in pregnancy

Hypertension in pregnancy, called a disease of degree is more of a sign than a disease by itself. With various advancements in the pathophysiology and various insights into the prevention of this disease, effective and timely control of hypertension is still the most imperative step in the management.

Concerns akin to maternal morbidity, mortality and fetal and neonatal outcomes imply the impact of the disease in the obstetric population.

The recent management option explores the various modalities in prediction and prevention of hypertension in pregnancy. However, the only effective therapy is the delivery of the fetus and placenta. The ancillary therapy is principally symptomatic and not directed at the fundamental cause.

Effective pharmacologic therapy modifies the course of the disease. The effective use of anti-hypertensive therapy should be based on well designed controlled clinical trials and the experience of the clinician with the drugs.

Hypertensive disorders complicate 5-10% of all pregnancies worldwide [1]. In India, pregnancy induced hypertension, along with sepsis and hemorrhages, contributes to 80% of the maternal mortality. Dangerous hypertension is a harbinger of

cerebrovascular accidents, eclampsia, hypertensive encephalopathy and other end organ damage with a poor perinatal outcome [2].

In order to mitigate the morbidity and the mortality, numerous antihypertensive agents are being used to control blood pressure in severe preeclampsia. Numerous reports signify that reducing severe hypertension reduces maternal death [3].

Antihypertensive drug in pregnancy should effectively reduce the blood pressure of the mother, should not cause acute hypotension, should not have any deleterious effects on the fetus in utero, and should not have any adverse interaction with other drugs including those commonly used in pregnancy and in labour. The use of the drug should modify the course of the disease and it should prevent the development of complications.

Hydralazine, diuretics and alpha methyl dopa are not recommended for use in severe hypertension as first line drugs due to adverse maternal, fetal outcomes and late onset of action of the latter.

Labetalol was studied for its use in treatment of hypertensive urgencies in the general population. The smooth onset of action with minimal change in cardiac output and heart rate makes it a unique drug in the management of hypertensive emergency in pregnancy.

Nifedipine has been evaluated for its immediate onset of action and ease of administration and no reported adverse effects on the mother or the fetus and on the course of labour.

This study ventures to compare the pharmacodynamics of intravenous labetalol and oral nifedipine in patients with severe hypertension and to compare the maternal and fetal outcomes and adverse effects of both the drugs.

AIM AND OBJECTIVE OF THE STUDY

A recent CEMACH report recommends urgent and effective anti hypertensive treatment for patients with severe hypertension in pregnancy [3].

Both intravenous labetalol and oral nifedipine [4] are used in acute blood pressure control in severe hypertension.

The aim of the study is to compare intravenous labetalol with oral nifedipine in the management of acute blood pressure control in hypertensive emergencies of pregnancy.

The present study is undertaken

- To study the efficacy and safety of intravenous labetalol and oral nifedipine
- To compare pharmacodynamics of intravenous labetalol and oral nifedipine including maternal and fetal side effect profile
- To evaluate the maternal and fetal outcome in both the groups

REVIEW OF LITERATURE

Definition

Hypertension in pregnancy goes by the definition of a sustained systolic blood pressure of 140 mm Hg or more and/or a diastolic blood pressure of 90 mm Hg or more detected for the first time during pregnancy after 20 weeks of gestational age. [5]

The working group classification of hypertension in pregnancy is as follows.

1. Gestational hypertension
2. Preeclampsia
3. Eclampsia
4. Preeclampsia superimposed on chronic hypertension
5. Chronic hypertension.

The minimal criteria for the diagnosis of preeclampsia are blood pressure of ≥140/ 90 mm Hg occurring after a gestational age of 20 weeks and presence of proteinuria ≥300 mg/day or ≥ 1+ in urine dipstick proteinuria examination.

The presence of the following features suggests the increased certainty of preeclampsia.

- Blood pressure of ≥ 160/110 mm Hg
- Proteinuria of ≥ 2g/day or a dipstick proteinuria estimation of ≥ 2+
- Newly detected rise in serum creatinine level of > 1.2 mg/dl
- Thrombocytopenia, with platelet count < 1,00,000/ µL
- Increased serum lactate dehydrogenase levels indicating microangiopathic hemolysis
- Elevated liver enzymes
- Persistent headache and visual disturbances
- Persistent epigastric pain

Severe preeclampsia is defined as severe hypertension with proteinuria or hypertension with severe proteinuria constituting 5 g/day or more. The definition includes multisystem involvement and also comprises imminent signs and symptoms. [6]

Epidemiology

Though mild disease occurs in about 2 to 7% of healthy nulliparous women, the incidence and severity of the disease are higher in high risk women. The risk factors may be couple, maternal or pregnancy related [7].

Risk factors

Couple related	Maternal risk factors	Pregnancy related risk factors
Primiparity Limited sperm exposure Paternal factors	Extremes of age Prior history of pregnancy induced hypertension Renal diseases Infections Susceptibility genes Family history Maternal infections	Multifetal gestation Hydropic degeneration of placenta Hydrops fetalis

Impact of pregnancy induced hypertension

80% of maternal mortality is associated with pregnancy hypertension when combined with anemia and post partum hemorrhage. Hypertension in pregnancy predisposes to maternal and fetal complication. Coexistent anemia worsens the picture of hypertension in pregnancy.

There is an increased incidence of placental abruption, preterm labour, preeclampsia, eclampsia, pulmonary edema, acute renal failure, intra cerebral hemorrhage and multi-organ failure.

The fetal outcome is also poor in terms of preterm births, intrauterine growth restriction, placental insufficiency, side effects of the drugs used to control blood pressure, increased incidence of operative deliveries and intra uterine demise. Such is the impact of the disease so that early detection, prompt referral, proper medical and obstetric management will give a good maternal and fetal outcome.

Pathogenesis

Named a disease of theories, the etiology of pregnancy hypertension is still an unknown arena compounding susceptibility factors, genetic predispositions, environmental factors and immunological dynamics.

The central elements predisposing to hypertensive state are-

- Exaggerated inflammatory response
- Inappropriate endothelial cell activation cascade
- Abnormally shallow endovascular cytotrophoblastic invasion in the spiral arteries

Endothelial cell activation

Endothelial cell activation has been found to be a key factor in the development of preeclampsia in recent studies. Gant and co-workers have postulated that activated endothelium expresses less nitric oxide and crafts the milieu in favour of procoagulant substances. The activated endothelium expresses various factors which brings about increased sensitivity to infused pressor agents [8].

Inflammation

Pregnancy is a state of systemic inflammation because of the shedding of syncytiotrophoblast cells in to the maternal circulation. If this shedding becomes excessive, maternal innate immune system is activated and preeclampsia ensues. Redman's two stage model of development of preeclampsia shows the role of placental ischemia-reperfusion injury. Recent studies point out that preeclampsia occurs due to certain auto immune disorders and infections including maternal periodontal diseases, urinary tract infections, Chlamydia and certain viral infections.

Immunology

Invasion of the trophoblast into the myometrium and decidua is controlled by the immune mechanism. The decidua contains lymphoid tissue, predominantly natural killer cells. The NK cells express KIR receptors, which recognize the HLA class I molecules. The NK cells secrete VEGF, PLGF, and Angiotensin 2 which bring about maternal placental bed vascular changes. Moffet King and colleagues studied the HLA C- NK cell receptor interaction. They state that each pregnancy is unique because of the NK cell- KIR- HLA C interaction. Mothers with absent or decreased KIRs which interact with HLA C group have increased propensity towards preeclampsia [9].

Balance between pro and antiangiogenic factors

Angiogenic factors like VEGF- A, PLGF are secreted by the villous, extra villous cytotrophoblasts, syncytiotrophoblast cells and decidual leukocytes. These factors induce the expression of nitric oxide and PGI_2 which bring about vasodilatation. sFlt-1 is a soluble version of VEGF receptor, which inhibits angiogenesis by reducing the circulating levels of VEGF and PDGF. Endoglin and sFlt-1 act in conjunction to bring

about endothelial dysfunction. Their levels are seen to be raised weeks before clinical manifestations of preeclampsia [10].

Pathophysiology

1. Cardiovascular system

In normal pregnancy, the plasma volume expands in the first and second trimesters up to 25%. Such an increase in plasma volume maintains fetal well-being. In women with severe preeclampsia, the rise in plasma volume is about 30 to 40% lesser than that of a normal pregnancy [11]. Such patients have increased propensity towards the occurrence of IUGR, oligohydramnios and preterm labour.

A sudden maternal weight gain of 1 kg/week or more over a period of two to three weeks or an increase in weight of more than 2 kg in one month is a dangerous harbinger of preeclampsia. The accelerated weight gain is due to the extracellular interstitial fluid collection as a result of a leaky microcirculation.

Normal pregnancy is constituted by rise in heart rate; decrease in systemic vascular resistance and thereby an increase in cardiac output in a sequential order. In severe preeclampsia, the state of high cardiac output- low systemic vascular resistance balance is tilted towards low cardiac output- high systemic vascular resistance state.

2. Renal system

Preeclampsia induces glomerular endotheliosis which is said to be the hallmark renal lesion in preeclampsia. Oliguria in preeclampsia is most often a consequence of glomerular endotheliosis, intrarenal vasoconstriction and hypovolemia. These functional derangements may progress to acute tubular necrosis. Preeclampsia is a major cause of obstetric acute renal failure. Acute renal failure in preeclampsia is most often due to acute tubular necrosis or rarely due to bilateral cortical necrosis in cases with severe preeclampsia. Prompt delivery is expedited in most instances.

3. Abnormal hemostasis

Endothelial damage incites platelet activation and adherence at the predisposed sites namely uteroplacental bed, renal and hepatic vasculature. Various studies show that thrombocytopenia is the most common hemostatic abnormality in preeclampsia. In severe preeclampsia, the platelet count seldom falls below 50000/cu.mm [12].

4. Liver

In severe preeclampsia, sinusoidal blood flow is obstructed by fibrin like material. This in turn brings about capsular distension, which manifests most commonly as malaise [13]. Non-specific viral syndrome like symptoms, epigastric distress, nausea and vomiting are other manifestations. HELLP syndrome, a variant of severe eclampsia, is heralded by hemolysis, elevated liver enzymes and low platelet count. It is caused by fibrin deposition in the arterioles which activate the coagulation system leading to lysis of erythrocytes and consumption of platelets. Liver suffers ischemia and hence periportal necrosis and subcapsular haemorrhages.

Though delivery is the definitive management, use of magnesium sulphate prophylaxis, corticosteroids, use of blood and blood products help in ameliorating the symptoms.

5. Brain

Recent data from Port JD and colleagues suggest that hypertensive encephalopathy and over perfusion of brain occurring in severe preeclampsia are the inciting events in eclampsia [14]. MRI studies of middle cerebral and posterior cerebral arteries show increased blood flow and Doppler studies show increased middle cerebral arterial velocity and increased cerebral perfusion pressure [15]. The prevention of acute severe rise in blood pressure thereby brings about a reduction in the morbidity and mortality of hypertensive patients. The use of anti- hypertensive medication thus prevents the

occurrence of hypertensive encephalopathy, over perfusion of the brain and other cerebral complications. Recent CEMACH review has also recommended the control of acute rise in blood pressure in pregnancy. [3]

Eclampsia is defined as the occurrence of convulsions and/or coma in women with either gestational hypertension or preeclampsia. The seizures are Grandmal in character and are predominantly tonic-clonic. Head ache (82.5%), visual disturbances (44.4%) and upper abdominal pain (19%) are the forerunners of eclampsia.

Hyperreflexia and clonus are said to be the hallmarks of severe preeclampsia. [16]

Maternal complications

Since hypertension in pregnancy is a multi organ disease, the complications involve almost all the organ systems. The patient may go in for eclampsia because of loss of cerebral auto regulation. The reported incidence is averaging 1 in 2000 deliveries. There is increased risk of operative deliveries and induction of labour done for the termination of the pregnancy. Abruption placenta occurs in about 1 to 4% of the patients.

Complete or partial HELLP syndrome may supervene, which has an incidence ranging from 10 to 20%. Coagulation dysfunction and full blown disseminated intravascular coagulation may occur. The raised systemic vascular resistance impairs the cardiac function leading to cardiac failure and pulmonary edema in about 2 to 5% of the patients. The risk of peripartum cardiomyopathy is increased. There is increased risk of adult respiratory distress syndrome probably due to management in high dependency unit with prolonged ventilator support.

Fetal and perinatal outcome

The outcome of the fetus or the neonate depends on the time of onset of hypertension and associated medical disorders. The incited prematurity can be iatrogenic or

spontaneous. The outcomes are favourable in pregnancies with the onset of hypertension after 36 weeks of gestation. On the other hand, prognosis is not good in pregnancies with early onset hypertension, with the occurrence of placental insufficiency, IUGR, oligohydramnios, operative deliveries, abruptio placenta, effects of drugs used to control hypertension and convulsions, to name a few.

The use of steroid to induce lung maturity in the case of preterm babies shows an improved outcome in terms of neonatal death, respiratory distress syndrome and intra ventricular hemorrhages. Fetal monitoring by cardiotocograph, non stress test biweekly and assessment of Doppler parameters weekly should be done.

Prognosis and long term sequelae

Severe preeclampsia is associated with a risk of 0.2% maternal mortality and 5% morbidity. The picture worsens with the occurrence of convulsions, endothelial dysfunction, vasospasm, small vessel thrombosis, intracranial haemorrhages, infarctions, acute tubular necrosis, multi-organ failure and coagulation abnormalities.

The persistence of hypertension longer than a period of 12 weeks is said to chronic hypertension. The Follow Up collaborative group of Magpie trial has shown that 20% of the hypertensive mothers were followed up to be chronic hypertensives. Such patients are at an increased risk of cardiovascular morbidity. The time of onset of preeclampsia has been found to have an impact on the recurrence of preeclampsia in the future pregnancies. In patients with early onset preeclampsia, the risk of recurrence of preeclampsia in the subsequent pregnancy is found to be around 40%, while those with a late onset disease had a risk of recurrence of 25%.

These patients have an increased propensity towards the development of ischemic heart diseases, neurovascular morbidity namely stroke, chronic renal disease and chronic hypertension.

Management options

The natural course of preeclampsia is blocked at the secondary and tertiary levels of prevention. While early detection and prevention of occurrence of the disease per se is called for, the allaying of the severity of the disease and thereby reducing the complications prompt the mainstay in the present times.

The morbidity and mortality of the preeclamptic mother and the neonate is considerably reduced with effective management.

Evidence based practice and setting up of a protocol in the management of acute onset, severe hypertension in preeclampsia and eclampsia bring about an immense encouraging outcome.

NICE guidelines state that intravenous or oral labetalol, oral nifedipine and intravenous hydralazine can be used as first line drugs in the management of severe preeclampsia. Consideration should be given for start of magnesium sulphate regime [17].

Consensus exists regarding the management of severe preeclampsia, which develops after 34 weeks of gestation. The patient is delivered by induction or caesarean section depending on the obstetric and fetal indications. [18]

Likewise, patients with a gestation of ≤ 34 weeks with imminent symptoms, signs of multi-organ dysfunction, non-reassuring fetal status, and eclampsia are delivered similarly [19].

Controversy exists over the management of severe preeclamptic patients of less than 34 weeks gestation with stable maternal and fetal indices. A recent review states that expectant management in a patient with severe preeclampsia at a gestational age between 24 and 33 weeks is a safe and a better practice and is said to bring about a

prolongation of pregnancy for 7 to 10 days. Such a management brings about a favourable neonatal outcome. [19]

The recommended criteria for termination of pregnancy for the patients on expectant management are as follows.

- Uncontrolled blood pressure
- Imminent signs and symotoms of eclampsia
- Non reassuring fetal cardiac status
- Oligohydramnios
- Oliguria
- Elevated renal parameters especially serum creatinine concentration
- Elevated liver enzymes
- Development of HELLP syndrome
- Pulmonary edema

In the case of pregnancies with severe preeclampsia with a gestational age of less than 24 weeks, the expectant management is said to give a high maternal morbidity with limited perinatal benefit. [20]

1. **General management**

The mainstay in the management relies on reduction of blood pressure, prevention of convulsions, with careful monitoring of input and output and fetal monitoring. Patients with severe preeclampsia are hospitalized. The patients should be monitored for blood pressure every fifteen minutes till reduction to a systolic blood pressure of 150 mm Hg and a diastolic blood pressure of less than 100 mm Hg.

Laboratory investigations including complete blood count including platelet count, liver enzyme study, coagulation profile and spot urine protein creatinine ratio for screening are undertaken. Fetal assessment with fetal heart rate monitoring, umbilical artery Doppler studies, ultra sonogram every two weeks are good practice principles.

A steroid for fetal lung maturity is indicated in pregnancies with less than 34 weeks gestation if delivery is awaited.

2. **Antihypertensive management**

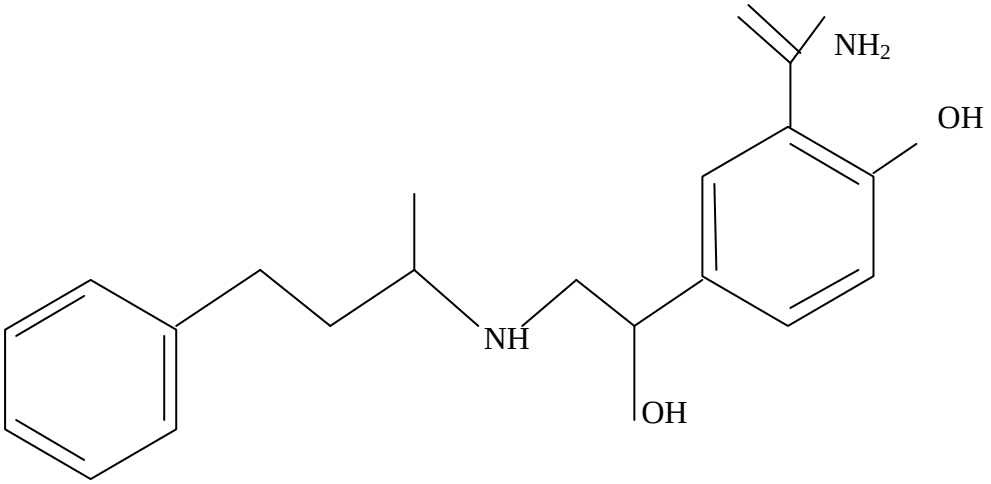
A wide armamentarium of drugs is available with various modes of administration, utilized for various indications. The most commonly used drugs are labetalol, nifedipine, alpha methyl dopa and hydralazine, to name a few. Gradual and prompt reduction of blood pressure in severe preeclampsia is warranted by the administration of intermittent dosage of drugs or by a continuous monitored infusion. Combinational use of drugs is not encouraged since their compound effect may bring about a hypotensive episode.

Consensus exists regarding the maintenance of blood pressure at 140 to 160 mm Hg systolic and 90 to 105 mm Hg diastolic range during the treatment of hypertension in pregnancy. A sudden steep decline of blood pressure is said to compromise the uteroplacental blood flow and thereby the fetus. The patient should be monitored for the anti hypertensive effect of the drug and occurrence of adverse affects in mother or the fetus. The dosage is modified according to the response.

Numerous studies are done comparing hydralazine with labetalol in acute blood pressure control. Since the former is associated with many poor outcomes namely increased caesarean sections, placental abruption and fetal heart rate abnormalities, the use of hydralazine is not recommended.

Many studies show the efficacy and rapidity of action of oral and intravenous labetalol in mild to moderate hypertension and acute severe hypertension of pregnancy respectively. Use of intravenous labetalol and oral nifedipine has found its place in the tertiary care protocol in the management of severe preeclampsia and eclampsia in most of the states in India.

Labetalol



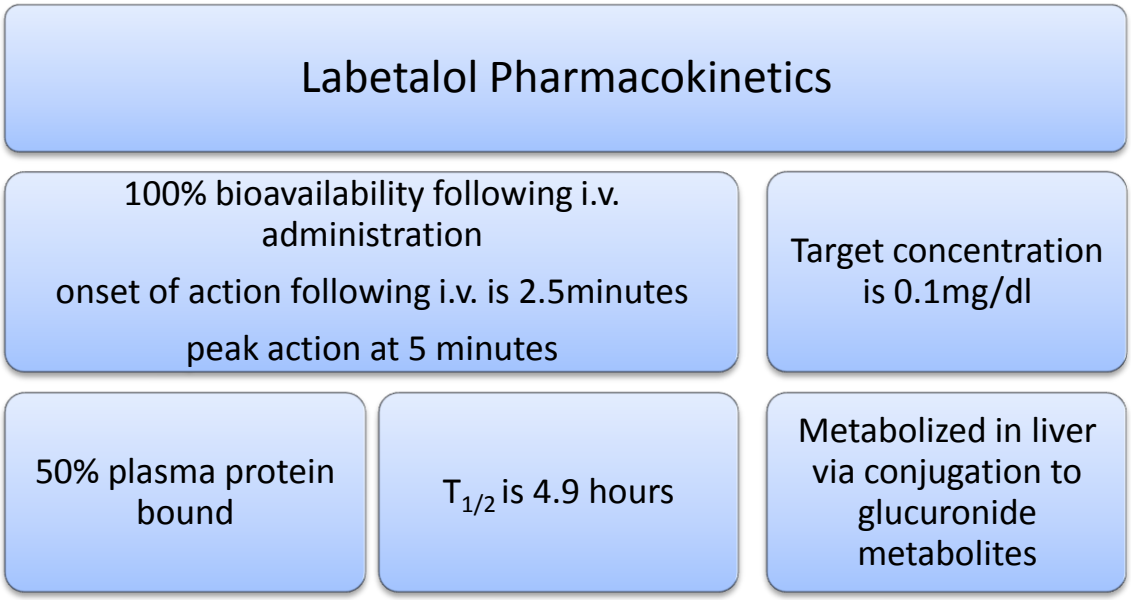
Labetalol, first of its kind, is a combined α- and β-adrenergic blocker. The chemical formulation contains four stereoisomers with distinct action profiles on the receptor subtypes. The available commercial preparation is a racemic mixture of two pairs of chiral isomers.

The ration of α to β blockade is 1: 7 following intravenous administration. The systolic and diastolic fall in blood pressure is attributed to both α_1 and β_1 blockade. Vasodilatation is brought about by β_2 weak agonistic activity.

The reduction in systemic vascular resistance with no change in heart rate and cardiac output is by α blockade. It reduces blood pressure smoothly and rapidly. There is a decrease in cardiac index following both oral and intravenous administration.

Labetalol is a pregnancy category C drug. It crosses the placenta and small amounts are secreted via breast milk. Sibai in his study prefers the use of labetalol [21]. The protocol issued by NHBPEP Working Group (2000) and American College of Obstetricians and Gynaecologists (2002) recommends the usage of 20 mg initial intravenous dose in the management of acute severe hypertension in pregnancy. The dose is doubled every ten minutes if there is no desired reduction in blood pressure till

a total dose infusion of 220 mg per episode. The use of 20 mg initial dose of labetalol is preferred since the target concentration is reached more readily.



Various studies conducted by Mabie and colleagues[22] and Vigil-De Gracia[23] and associates highlight the rapid action, better maternal and neonatal outcomes and minimal side effect profile of intravenous labetalol in comparison with intravenous hydralazine in antepartum and postpartum phases respectively. Lower doses were found to be effective for hydralazine group though with higher reporting of maternal and fetal adverse effects namely operative interventions, abruption placenta and fetal distress respectively. The above mentioned trial showed that labetalol is a safe and effective alternative drug when compared to hydralazine.

In addition to its usage by intermittent bolus doses, Walker and co-workers recommend intravenous infusion regimen of labetalol as a second line treatment in the control of acute severe hypertension in pregnancy [24].

Adverse reactions, contraindications and drug interactions

The most commonly reported adverse effect is dizziness reported in about 20% of the patients. Other common adverse effects are nausea, fatigue, and light headedness. Since postural hypotension is common, left lateral positioning of the patient is advised when administering the drug intravenously.

The usage of this drug is contraindicated in patients with obstructive airway diseases including bronchial asthma, cardiac failure and heart blocks. Caution is advised in the usage of drug in impaired liver function, diabetes mellitus and cardiac failure [25].

Labetalol is associated with a smooth and rapid reduction in blood pressure. The administration can be through continuous infusion or intermittent regime. Adequate control of hypertension can then be followed by the intake of the drug via the oral route. The use of intravenous route entails prompt onset of action, adequate monitoring and dose titration.

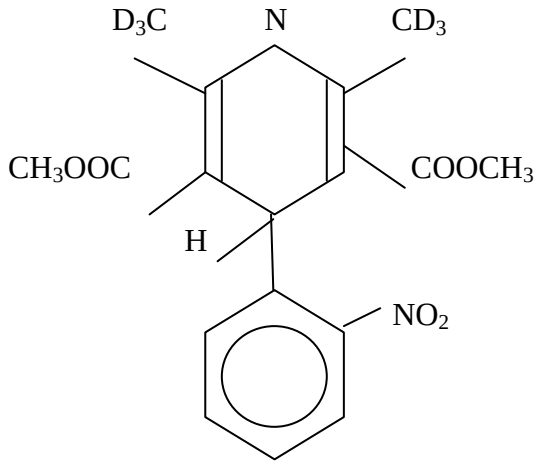
The drug does not have any adverse impact on the maternal systems, neonatal outcome, mode of delivery and further complications from the disease per se. Drug combinations are generally avoided in pregnancy hypertension for fear of interactions and drastic reduction in blood pressures. When labetalol is used along with nifedipine, monitoring is essential to avert a sudden fall in blood pressure. [26]

Anti hypertensive drugs tend to compromise the placental circulation. No change in the umbilical blood flow is noted following the usage of labetalol according to the study by Baggio and co-workers [27]. Hydralazine increased uterine artery resisitance index and labetalol did not have a significant adverse fetal circulatory disturbances.

A clinical trial by Michael et al reports the accelerated fetal lung maturity by the usage of labetalol though further confirmatory studies are warranted [28]. The use of labetalol in hypertensive pregnant patients who were taken up for caesarean section

showed a decreased hypertensive response and reflex laryngospasm on intubation during general anesthesia [29].

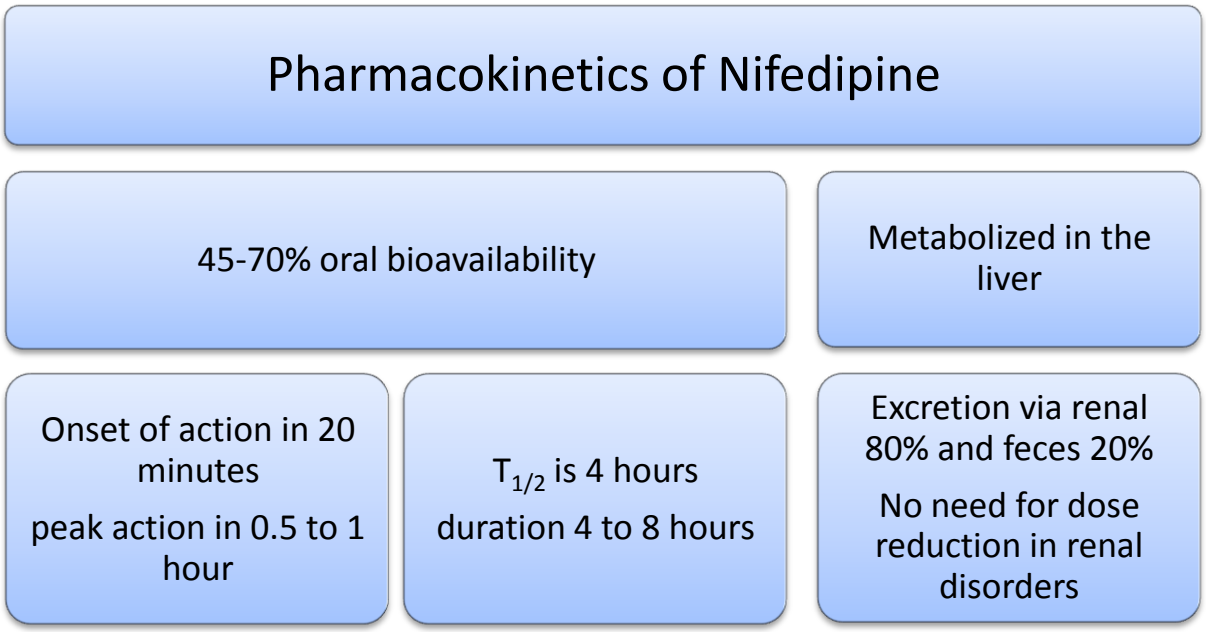
Nifedipine



It was discovered as early as 1800 that calcium influx is an essential part in smooth muscle contraction. Henceforth, L type calcium channel blockers are used in various indications. Nifedipine, a prototype of dihydropyridine group of calcium channel blockers has been studied extensively for its utility in hypertensive disorders of pregnancy.

The use of the drug has been established both in mild to moderate hypertensive disorders of pregnancy and severe preeclampsia for acute blood pressure control.

Calcium channel had four subtypes of receptor, nifedipine is said to block the α_1 subtype and thus reduces the transmembrane calcium current, thereby producing a long lasting smooth muscle relaxation. [30]



Nifedipine effectively dilates the arterioles in preference to veins thus producing an effective vasodilatation without producing postural hypotension. It reduces the total peripheral resistance and thereby reduces the after load. This effect may produce an inconsequential amount of reflex tachycardia. There is a small increase in cardiac index. It has a rapid onset of action by oral route. The drug is available in immediate release and extended release tablets and capsules. The oral route provides an ease of administration without compromising the efficacy. The site of absorption of oral nifedipine is at the duodenum and jejunum. The gastric emptying time of pregnant women is found to be the same as in the non pregnant. However, there is a delay in the gastric emptying time during labour most often due to the use of analgesics. The elimination half life of nifedipine is said to be shortened with pregnant women implying a frequent dosing for a better anti hypertensive effect. Thus it shows that the oral route of administration is adequate enough to give a prompt onset of action in the blood pressure control. Sublingual route is not recommended since it produces a rapid fall of the blood pressure. NICE guideline recommends the use of oral nifedipine in blood pressure control in eclampsia and severe preeclampsia.

In a study conducted by Sibai et al the use of nifedipine has been compared with bed rest in pregnancy induced hypertension. The use of nifedipine has been shown to effectively reduce both systolic and diastolic blood pressure. However, there was no improved outcome in terms of prolongation of pregnancy or the fetal outcome [31].

The antihypertensive effect was compared with placebo in a trial by Ismail et al [32], which shows that the mean arterial pressure was effectively reduced in nifedipine group and the drug brought about an increased urine output because of the vasodilatory effect.

The use of nifedipine has been found to be effective and predictable in the trial by Fenakel et al. There was no drastic hypotensive response with the oral route. The study implies that nifedipine is superior to hydralazine [33].

Nifedipine is a pregnancy category C drug. The drug crosses the placenta. There is no reported change in the uteroplacental blood flow. About 5% of the drug is secreted in the breast milk producing little or no neonatal hypotension.

Adverse reactions, contraindications and drug interactions

The most commonly reported adverse effects are ankle edema (10-30%), flushing (25%), dizziness (25%) and headache (10- 20%) [34]. The only contraindication to its administration is hypersensitivity to the drug.

Certain case reports warn about the theoretical interaction between magnesium sulphate administrations along with nifedipine. Both the drugs exhibit phamacodynamic synergism when administered together producing hypotension and neuromuscular blockade warranting close monitoring [35, 36]. However, the renowned Magpie trial involving 10141 women with preeclampsia had 3029 women with concomitant magnesium sulphate and nifedipine administration. There was no significant hypotension or neuromuscular blockade reported in the study [37].

The comparison of efficacy, duration of action and side effect profile of both the first line drugs namely labetalol and nifedipine in the management of severe preeclampsia can bring about better outcomes in the mother and the fetus.

Alpha methyldopa

Methyldopa, with an established long term safety [38], is an effective drug as a monotherapy in mild to moderate hypertension reducing the progression to severe preeclampsia. However, it is not useful in severe hypertension. The mechanism of action is by reduction of overall sympathetic outflow. The onset of action is in 4 to 6 hours. It is metabolized in the liver and excreted through the kidney. The most common side effect is postural hypotension; excessive sedation and depression are also seen.

Hydralazine

Hydralazine acts by direct peripheral vasodilatation. It was the drug of choice in hypertensive emergencies in the past. The onset of action is 10 to 20 minutes. It produces significant hypotension producing no reassuring fetal cardiac status and fetal distress [39]. The proposed mechanism is by release of noradrenaline.

Magee et al in a meta-analysis reported worse maternal and fetal outcomes with hydralazine when compared to both nifedipine and labetalol, thus no longer recommending its use. There was an increased association of maternal hypotension (RR 3.29, 95% CI 1.50- 7.23), caesarean section (RR 1.30, 95% CI 1.08- 1.59), placental abruption (RR 4.17, 95% CI 1.19- 14.28), maternal oliguria (RR 4.00, 95% CI 1.22- 12.50) and low Apgar scores (RR 2.70, 95% CI 1.27- 5.88) following the use of hydralazine [40].

Diazoxide

Diazoxide is a benzothiazine derivative that acts by direct vasodilatation producing a rapid and long lasting effect. Since its usage is associated with maternal cerebral ischemia, maternal death and fetal distress [41], it is recommended only in extremely high blood pressures. Recently the use of minibolus doses of diazoxide constituting 15 mg has no associated profound maternal hypotension [42].

Sodium nitroprusside

This drug has been used as a last resort in reducing high blood pressures. It acts by release of nitric oxide, which has vasodilator effects. It has a rapid onset of action, associated with the risk of rebound hypertension. Cyanide toxicity is reported in the fetus following its administration. The current usage, is hence limited to post partum usage or immediately prior to the delivery. [5]

Nicardipine

A calcium channel blocker, nicardipine is evaluated as a second line antihypertensive agent in pregnancy. Cabonne and colleagues studied the usage of nicardipine in the management of hypertension [43]. The drug needs careful monitoring for possible renal shut down.

Diuretics and other drugs

Since diuretics can compromise the placental blood flow, the usage is solely limited in the management of pulmonary edema. Zeeman and co-workers, in their study elucidated that use of diuretics reduces an already depleted intravascular volume [44].

Various other drugs like nimodipine, verapamil, intravenous ketanserin, and experimental drugs like calcitonin gene related peptide and cardiotonic steroids have also been evaluated for their utility in pregnancy hypertension.

The use of ACE inhibitors is contra indicated in pregnancy because of teratogenecity, growth retardation, and respiratory distress syndrome.

3. Seizure prophylaxis

Magnesium sulphate, with its neuroprotective and anticonvulsant properties has been compared extensively with other anticonvulsants or a placebo for its use in seizure prophylaxis and control of seizures [36, 45]. In the Magpie trial, magnesium sulphate reduced the risk of eclampsia by 58% compared to placebo. The American College of Obstetricians and Gynecologists recommend the use of prophylactic magnesium sulphate in severe preeclampsia [46].

Debate continues as regards the use of magnesium sulphate only to patients with an eclamptic seizure. But, a wider opinion is in favour of prophylactic treatment taking into account the significant mortality and long term morbidity of the mother and the neonate associated with the disease. However, universal prophylaxis is of no benefit. Alexander and associates issued a protocol considering the criteria based on National High Blood Pressure Education Program Working Group and the American College of Obstetricians and Gynecologists [47].

The selective use of magnesium sulphate prophylaxis is indicated in any woman with new onset proteinuric hypertension, and including at least one of the following criteria.

- Systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥ 110 mm Hg
- Proteinuria by dipstick measurement ≥ 2 +
- Serum creatinine > 1.2 mg/dl
- Platelet count < 100000/ cu. mm.
- Aspartate transaminase elevated twice the upper limit of the normal value
- Persistent headache or scotoma
- Persistent mid epigastric or right upper quadrant pain

Magnesium sulphate crosses the placenta and brings about a better outcome in the neonate. It is said to provide a cerebro-protective effect in the neonate, thereby reducing the incidence of cerebral palsy.

The recommended dosage by Pritchard regime is constituted by loading dose and maintenance doses of 20% and 50% magnesium sulphate respectively. The loading dose of 4 gram by the intravenous route by which the drug is given over a period of not less than 10 minutes, along with 10 gram of the 50% drug administered intramuscularly at both buttocks.

The maintenance dose involves alternate 5 gram 50% drug intramuscular injections at an interval of four hours on alternate buttocks. The drug regime is continued for 24 hours past the delivery of the baby or 24 hours past the last fit in the case of eclampsia, whichever is later.

Patients who are given magnesium sulphate are monitored for symptoms of magnesium toxicity namely loss of deep tendon reflexes, oliguria and respiratory depression.

4. Fluid management

Preeclampsia is a state of intra vascular fluid depletion. The knowledge of fluid management comes from invasive hemodynamic monitoring in preeclampsia and in compromised states such as pulmonary edema, cardiac failure and renal shut down. The state of volume depletion with decreased cardiac output coupled with low oncotic pressure and capillary damage predisposes to pulmonary edema. The condition is further deteriorated by the injudicious use of volume expanders. The American College of Obstetricians and Gynecologists recommend invasive hemodynamic monitoring in severe cardiac disease, renal disorders, renal shutdown, refractory hypertension and pulmonary edema [45].

Central venous pressure monitoring and Swan Ganz catheter insertion provide information regarding right ventricular and left ventricular functions respectively. Central venous pressure monitoring is validated in the correction of hypovolemia prior to antihypertensive therapy. Crystalloids are recommended in comparison to colloid administration. Lactated Ringer solution is administered at the rate of 60 ml to 125 ml per hour in volume depleted states. Swan Ganz catheter is useful in conditions like pulmonary edema, uncontrolled hypertension, severe oliguria and multi organ failure. Both the procedures are associated with risks namely cardiac arrhythmias, pulmonary infarction and pulmonary hemorrhage.

5. Steroids for lung maturity

Accelerated lung maturity does not occur in preeclampsia [48]. The perinatal outcome is dependent on the gestational age at the time of delivery. Corticosteroid treatment significantly reduced the neonatal morbidity and mortality in term of reduced neonatal death, respiratory distress syndrome and cerebro vascular hemorrhage [49]. The benefit is limited to usage before 34 weeks of gestation.

6. Fetal surveillance

The protocol of fetal surveillance should be based on individual obstetric units as there is no consensus on the same. Correct assessment of gestational age, clinical examination and radiographic evaluation are the mainstay in the evaluation. The various modalities used are biophysical profile, assessment of amniotic fluid volume, cardiotocography and Doppler studies. No single modality is said to be superior to the other. Moreover, acute events like placental abruption or cord accidents cannot be predicted by these modalities. By far, the only surveillance modality that has shown to reduce the need for intervention is the umbilical artery Doppler velocimetry.

7. Labour and delivery

The only cure for severe preeclampsia is termination of pregnancy [50]. After stabilization of the blood pressure and providing adequate time for the corticosteroid to act so as to accelerate the fetal lung maturity, the patient should be promptly delivered by induction or caesarean section depending on the obstetric indication. The decision towards caesarean section depends on fetal condition, obstetric indications, Bishop Score and presence of labour. Various reports indicate that immediate or elective caesarean section confers no benefit [51]. Induction of labour and vaginal delivery is not associated with adverse neonatal outcome [52]. Oxytocin is administered during the active management of the third stage of labour. Ergometrine is contraindicated since its use is associated with cerebral vasospasm and hypertensive crisis. Monitoring of blood pressure, fluid balance and assessment of blood loss during delivery and adequate replacement is mandatory in hypertensive patients.

8. Anesthetic considerations

General practice principles recommend early involvement of anesthetists in patients with severe preeclampsia. The issues in consideration are anesthetic risk assessment, control of blood pressure, fluid management, seizure prophylaxis and anesthetic or analgesic considerations. Patients with organ failure require high dependency setting. Epidural anesthesia serves as a good adjunct to vaginal delivery by improving the renal and uteroplacental blood supply. The drugs to be avoided are ergometrine, ketamine and NSAIDs. Regional anesthesia is used in preference to general anesthesia. Close monitoring of vital signs is advised to avoid neuromuscular blockade in patients receiving magnesium sulphate regime. Low dose aspirin treatment is not a contraindication to regional anesthesia. Platelet count of less than 50000/ cu. mm. is a contraindication for regional anesthesia.

9. Postpartum management

Seizure prophylaxis should be continued for 24 hours post partum since ≤44% of eclampsia is said to occur in the postpartum period. Anti-hypertensive drugs should be continued in the post partum period. The dosage is titrated according to the blood pressure control. Fluid balance monitoring, evaluation of hepatic, renal function and neurological status is validated. Since preeclampsia is a risk factor for thrombosis, thromboprophylaxis is administered unless surgically contraindicated. In-hospital stay, obesity, nephritic range proteinuria and operative delivery predispose to thrombosis.

10. Follow up

Patients requiring medication for the control of blood pressure should be frequently reviewed. Since these patients are at an increased risk for adverse cardio vascular events, they should be under surveillance. Preconception counselling should be advised in the next pregnancy. Early onset severe disease should be evaluated for the presence of antiphospholipid antibody syndrome and further screening for thrombophilia if indicated [53]. Contraceptive advice should also be provided.

MATERIALS AND METHODS

Materials and methods

The study was conducted in a tertiary care teaching institution, Mahatma Gandhi Memorial Government Hospital, Tiruchirapalli in the Department of Obstetrics and Gynecology during the period of November 2012 to November 2013. Ethical committee clearance was obtained.

One hundred and six consecutive patients satisfied the inclusion criteria and were recruited in the present study.

Inclusion Criteria

- Age – 18 to 35 years,
- All pregnant women of 20 weeks gestation or more; excluding parity and booking status
- Singleton pregnancy
- Sustained severe hypertension: Systolic blood pressure ≥ 160 mm Hg ; diastolic blood pressure ≥110 mm Hg; or a mean arterial pressure of > 125mmHg, lasting for 15 minutes or more in the past 4 hours on at least 2 occasions.
- Severe pre-eclampsia according to the consensus by the national high blood pressure education program, NHBPEP 2000.

Exclusion Criteria

- Eclampsia; HELLP syndrome
- Bronchial asthma
- Cardiac failure
- Cardiac rhythm abnormalities
- Chronic hypertension
- Co-existent diseases like diabetes mellitus, rheumatic heart disease, congenital heart disease, renal or hepatic disorders
- Multiple pregnancy
- Exposure to either drugs prior to the study

Study design

This study is a prospective randomized double blind comparative clinical trial with randomization done using computer generated numbers.

History

A thorough history was elicited from the patients regarding age, parity, socio economic status, booking history, history suggestive of imminent symptoms. Their past history regarding bronchial asthma, cardiac diseases, prior drug intake for hypertension and other medical disorders were also obtained.

Clinical examination

A meticulous general examination and obstetric examination were carried out. On general examination, patients' level of consciousness, degree of anemia, edema, jaundice, pulse rate, respiratory rate and temperature were ascertained.

Blood pressure measurement was done with the mercury sphygmomanometer with the patient lying at an angle of 45 degrees. The mercury manometer placed at the level of patients' heart. The measurements were taken in the right arm. The fifth Korotkoff,

K5 sound was taken for diastolic blood pressure cut off. When K5 was not heard, muffling of the sound, K4 was considered.

Systemic examination and obstetric examination were carried out. Fetal wellbeing was ascertained with the use of cardiotocograph before and after the usage of anti-hypertensive agents and other drugs.

Investigations

- Urine analysis
- Complete blood count including platelet count
- Blood grouping and typing
- Renal function tests
- Liver function tests
- Peripheral smear study
- Serum lactate dehydrogenase level
- Ultrasonogram
- Cardiotocograph

Anti-hypertensive management

After explaining the condition of the patient and getting prior informed consent, the pregnant women were randomized with computer generated numbers into two groups to receive either oral nifedipine or intermittent intravenous labetalol injections.

Group A

Fifty three patients were selected consecutively according to random numbers to receive the package containing intravenous labetalol injection in escalating doses of 20 mg, 40 mg, 80 mg, 80 mg, 80 mg and a placebo tablet for every fifteen minutes until the target blood pressure of $\leq 150 / \leq 100$ mm Hg was achieved.

Group B

Fifty three patients were randomized to receive the package containing nifedipine 10 mg tablet orally and intravenous placebo saline injections of 4 ml, 8ml, 16 ml, 16 ml, 16 ml up to five doses, every fifteen minutes till the target blood pressure of ≤ 150 / ≤ 100 mm Hg was achieved.

The drug regime was crossed over to the other group if the initial regime was found unsuccessful after five cycles and blood pressure monitoring done. Patient was made to rest in bed in left lateral position. Blood pressure was noted every 15 minutes. Once the blood pressure was <150 / 100 mm Hg, no further trial medication was given until two consecutive readings were > 160/ 110 mm Hg.

After successful control of blood pressure, further antihypertensive therapy was started two hours after the last trial medication.

Obstetric management

A careful obstetric examination was carried out. Bishop's score was calculated. Fetal status is ascertained by cardiotocograph. Delivery of the fetus and placenta was expedited according to individual condition of the patients. Induction of labour was done with intra-cervical PGE_2 gel instillation. Acceleration of labour was done with intravenous oxytocin infusion. Caesarean section was done for obstetric, fetal indications and failed inductions.

Maternal side effect profile was recorded. Neonatal monitoring included number of admissions in the neonatal intensive care unit, occurrences of hypotension and hypoglycaemia.

During the course of trial, maternal heart rate and fetal heart rate was monitored every 15 minutes. The trial was abandoned when there was non-reassuring fetal status and if maternal complications like hypotension, chest pain occurred.

Outcome measures

The primary outcome of this trial was the time taken to achieve a target blood pressure of ≤ 150 mm Hg systolic and ≤ 100 mm Hg diastolic in both the groups. Both had to be achieved.

The secondary outcome measures include total number of antihypertensive doses to achieve the target blood pressure, both systolic and diastolic, any cardio-tocographical abnormality, and maternal heart rate profile in the first hour, maternal hypotension, side effect profile and perinatal outcomes.

After completion of the trial protocol, patients were asked to complete a questionnaire with yes or no answers on the symptoms of nausea, palpitation, flushing, dizziness, headache, and shortness of breath experienced.

Statistical analysis

All the data were entered consecutively in a predefined data information sheet and analysis was done using SPSS 20 software. Differences in categorical and continuous data were assessed using the Chi square test and Student‘t’ test, respectively. The tests were two sided. The statistical test is considered significant if the calculated p value is less than 0.05.

ANALYSIS OF RESULTS

TABLE – 1

AGE DISTRIBUTION

S. NO.	AGE	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	≤ 20 YEARS	10	18.90%	13	24.5%	23 (21.70%)
2.	21 to 29 YEARS	34	64.10%	32	60.4%	66 (62.30%)
3.	≥ 30 YEARS	9	17%	8	15.1%	17 (16%)
MEAN (S.D.)		24.89 (4.25)		24.81 (4.22)		
STATISTICAL INFERENCE		T = 0.092 Degree of freedom = 104 P = 0.927				

There is no significant difference in ages of the recruited patients in both the groups. The mean age in labetalol and nifedipine groups was 24.89 and 24.81 years respectively. The majority of the patients had an age belonging to the category of 21 to 29 years. 18.90 % and 24.50% from group A and group B respectively had ages 20 years and below.

FIGURE – 1

AGE DISTRIBUTION

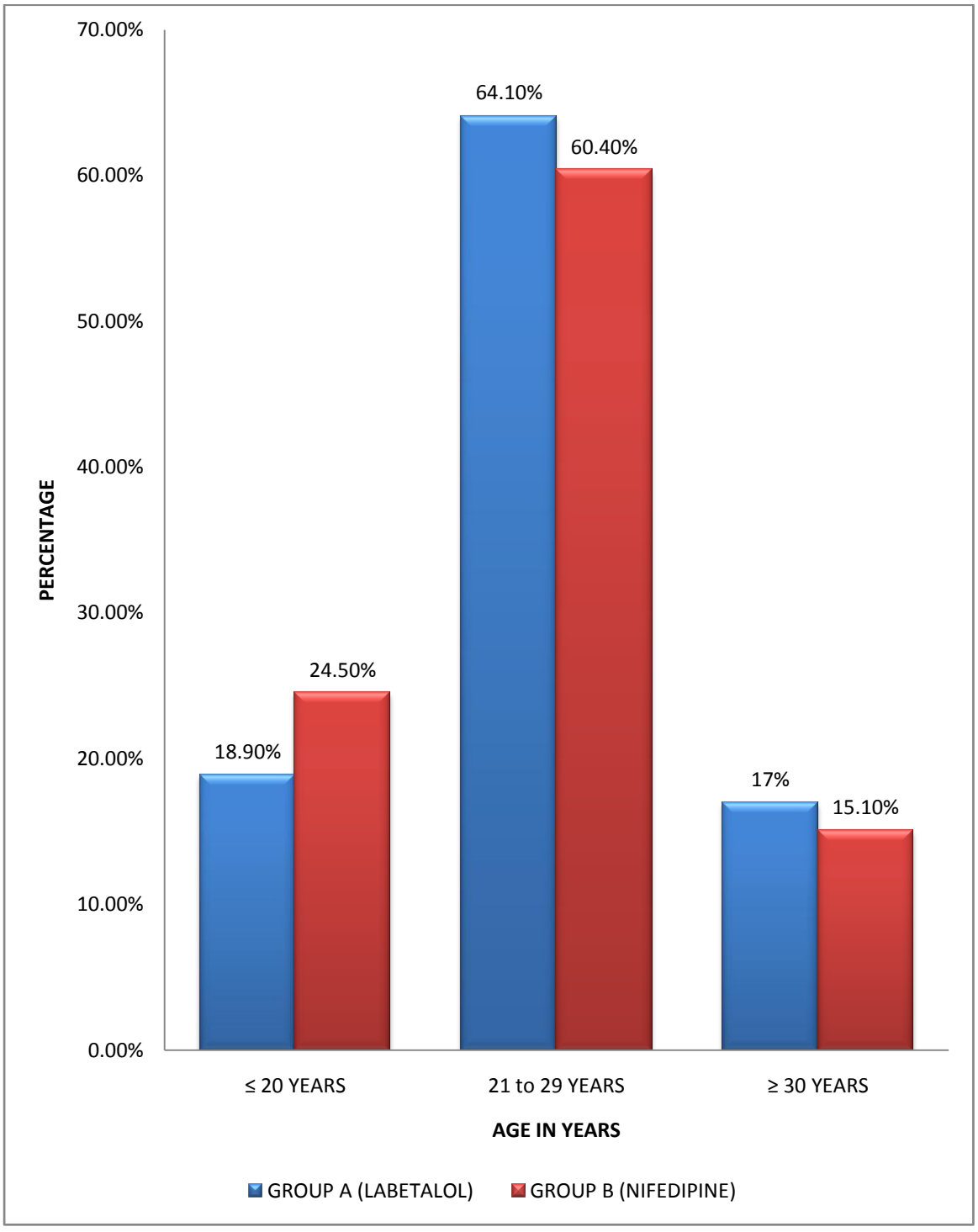


TABLE – 2

PARITY

S. NO.	PARITY	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	PRIMI	40	75.47%	27	50.94%	67 (63.20%)
2.	G2	7	13.20%	13	24.53%	20 (18.90%)
3.	G3	3	5.66%	9	16.98%	12 (11.30%)
4.	G4	3	5.66%	4	7.55%	7 (6.60%)
STATISTICAL INFERENCE		χ^2=7.465 Degree of freedom = 3 P= 0.058 > 0.05				

Parity was comparable in group A and group B. There is no significant difference in the parity of both the groups. Majority of the patients constituting 75.47% of group A and 50.94% of group B were primigravida. 63.20% enrolled in the study were primigravida. There is a higher incidence of preeclampsia in the first pregnancy.

FIGURE – 2

PARITY

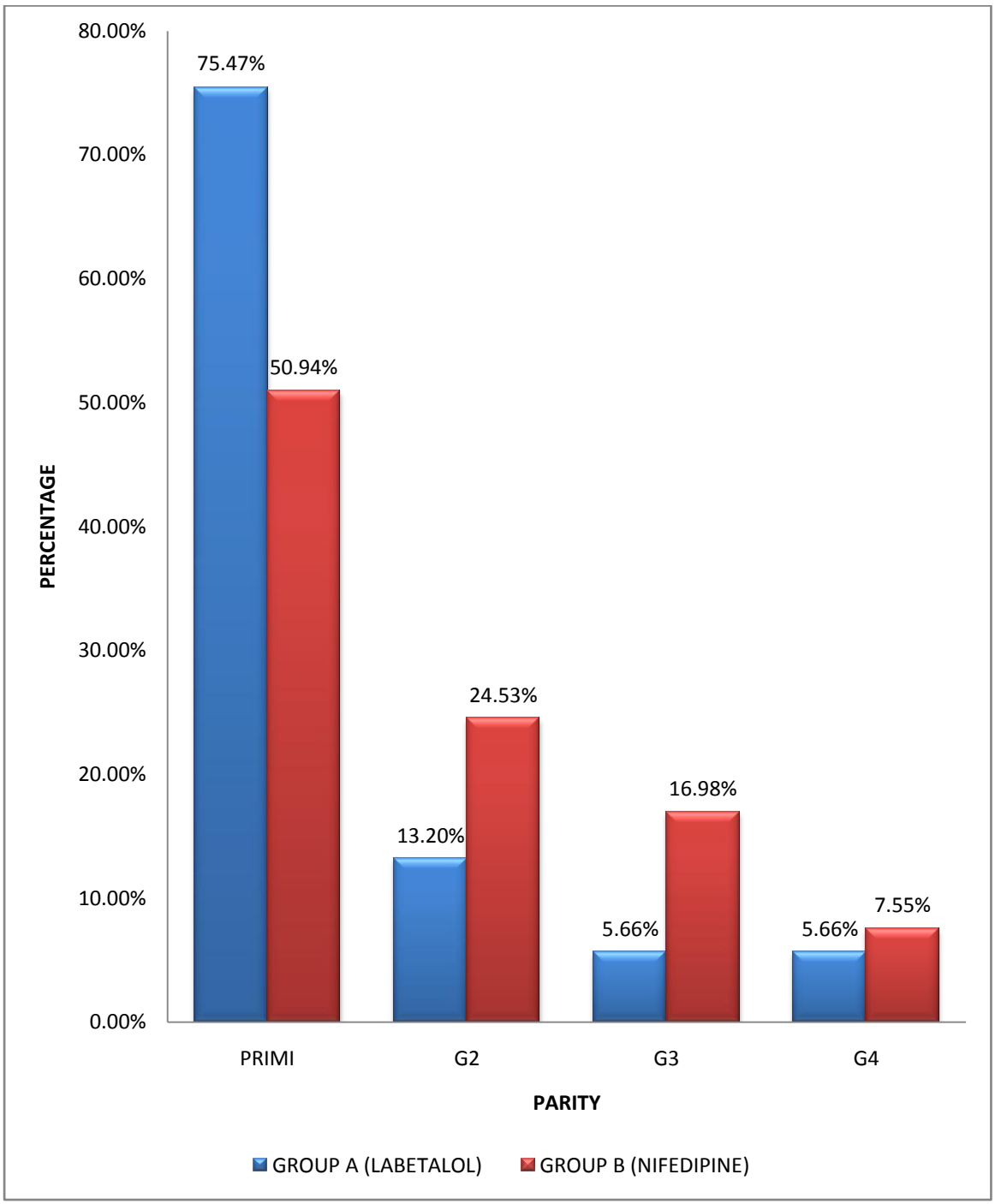


TABLE – 3

BOOKING STATUS

S.NO.	BOOKING STATUS	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	Booked	30	56.60%	28	52.80%	58(54.70%)
2.	Unbooked	23	43.40%	25	47.20%	48(45.30%)
STATISTICAL INFERENCE		$\chi^2 = 0.152$ Degree of freedom = 1 0.696 > 0.05				

The antenatal booking status did not differ significantly in both the groups. 43.40% and 47.20% from group A and B respectively were unbooked**.**

FIGURE – 3

BOOKING STATUS

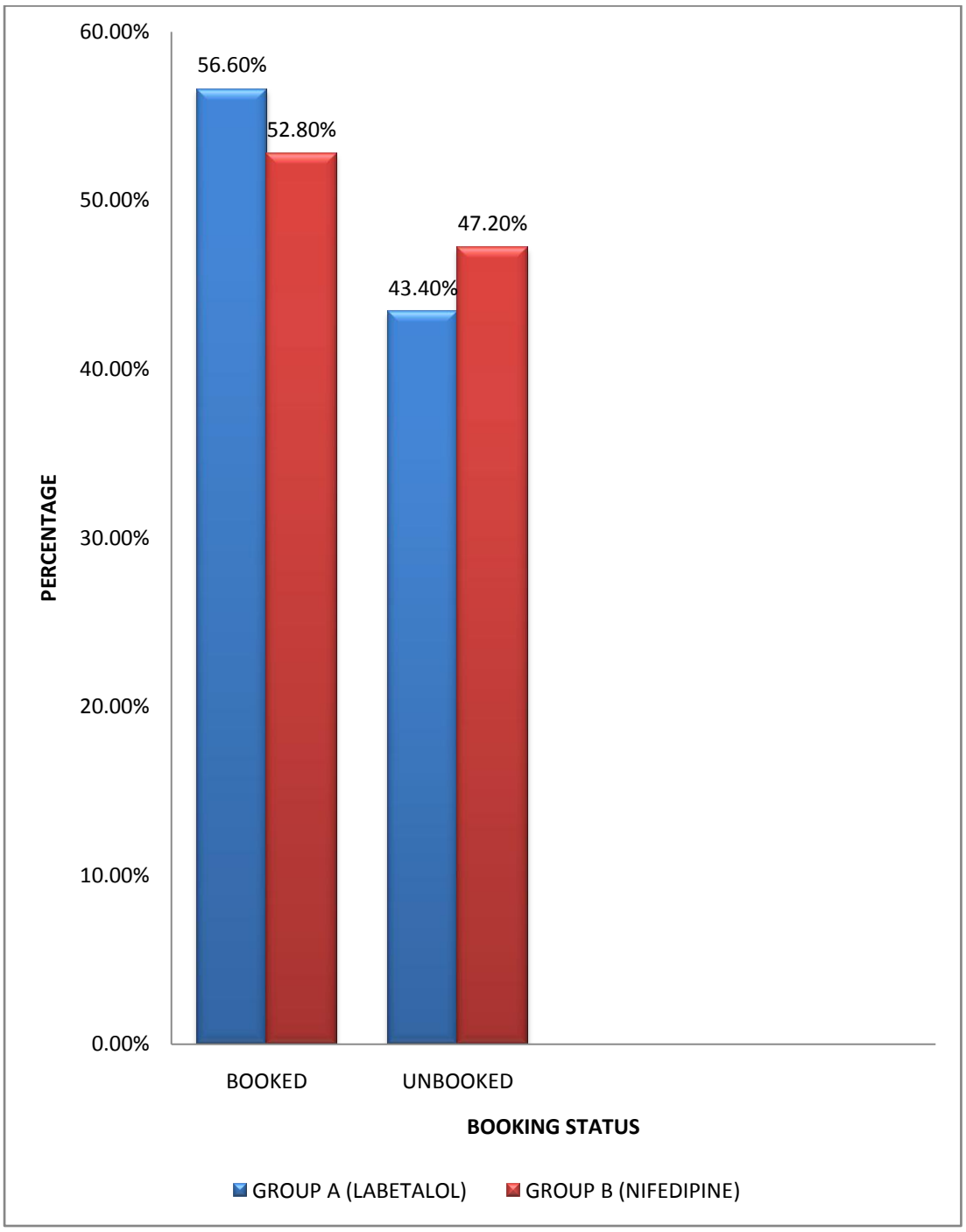


TABLE – 4

GESTATIONAL AGE

S. NO.	GESTATIONAL AGE	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	≤ 24 WEEKS	1	1.89%	2	3.77%	3 (2.83%)
2.	25 to 28 WEEKS	7	13.21%	6	11.32%	13 (12.26%)
3.	29 to 33 WEEKS	19	35.85%	17	32.08%	36 (33.96%)
4.	34 to 36 WEEKS	22	41.51%	21	39.62%	43 (40.57%)
5.	≥ 37 WEEKS	4	7.55%	7	13.21%	11 (10.38%)
STATISTICAL INFERENCE		$\chi^2 = 1.363$ Degree of freedom = 4 P = 0.851 > 0.05				

3 of the recruited patients, 1 in group A and 2 in group B had early onset disease at gestational age less than 24 weeks. The majority of the patients had gestational age of 34 to 36 weeks constituting 43% on the whole with 41.51% and 39.62% respectively in group A and B. The recruited patients did not significantly differ in gestational age.

FIGURE – 4

GESTATIONAL AGE

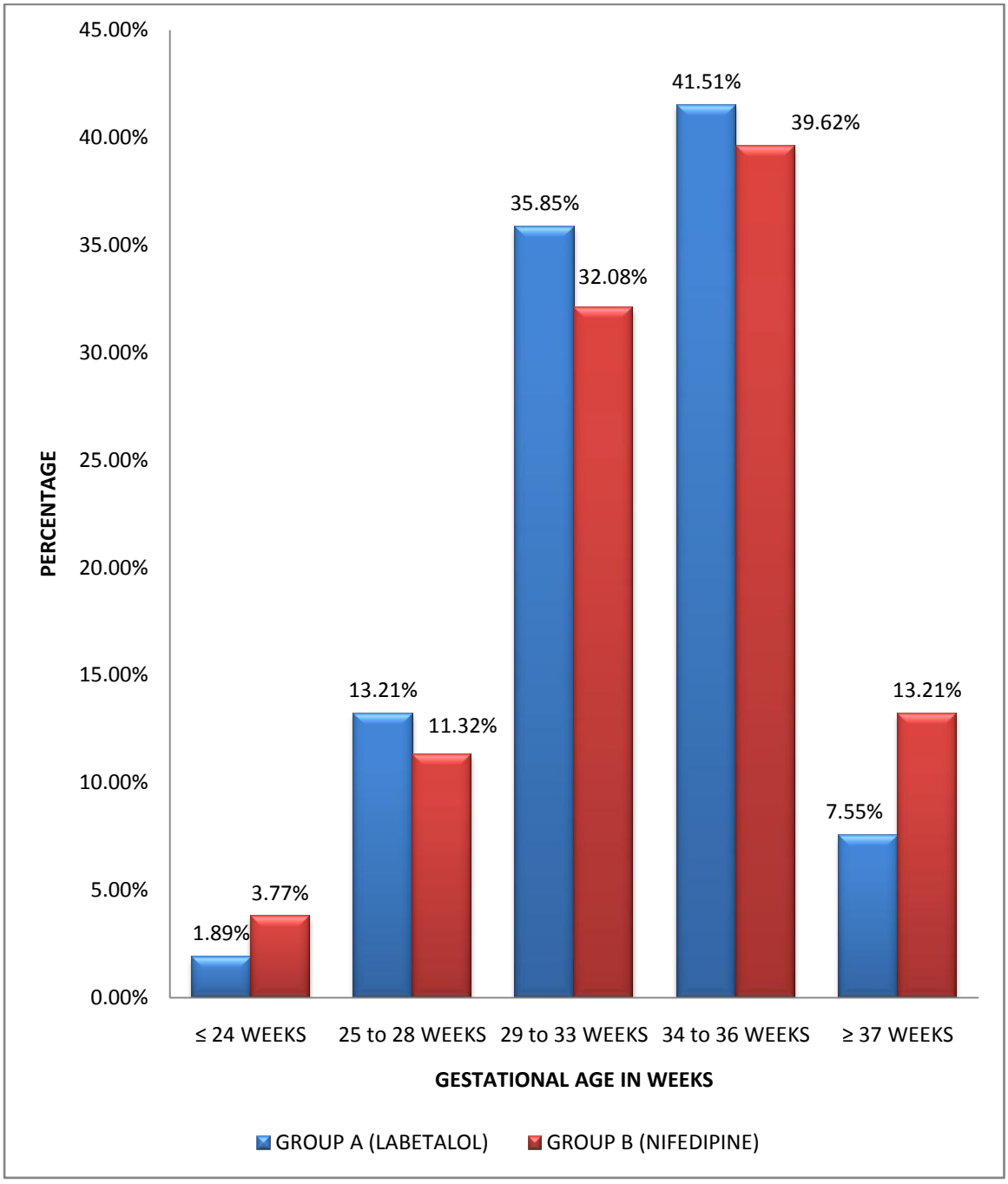


TABLE – 5

BODY MASS INDEX

S.NO	BODY MASS INDEX	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	25 to 29.99 kg/m^2	20	37.70%	20	37.70%	40 (37.70%)
2.	$\geq$ 30 kg/m^2	33	62.30%	33	62.30%	66 (62.30%)
MEAN (S.D.)		30.93 (2.33)		30.90 (2.18)		
STATISTICAL INFERENCE		χ^2=1.000 Degree of freedom = 1 1.000 > 0.05				

Most of the patients namely 66, constituting 63.30% had a body mass index exceeding 30 belonging to the category obesity. There is no significant difference in the body mass index between the two groups.

FIGURE – 5

BODY MASS INDEX

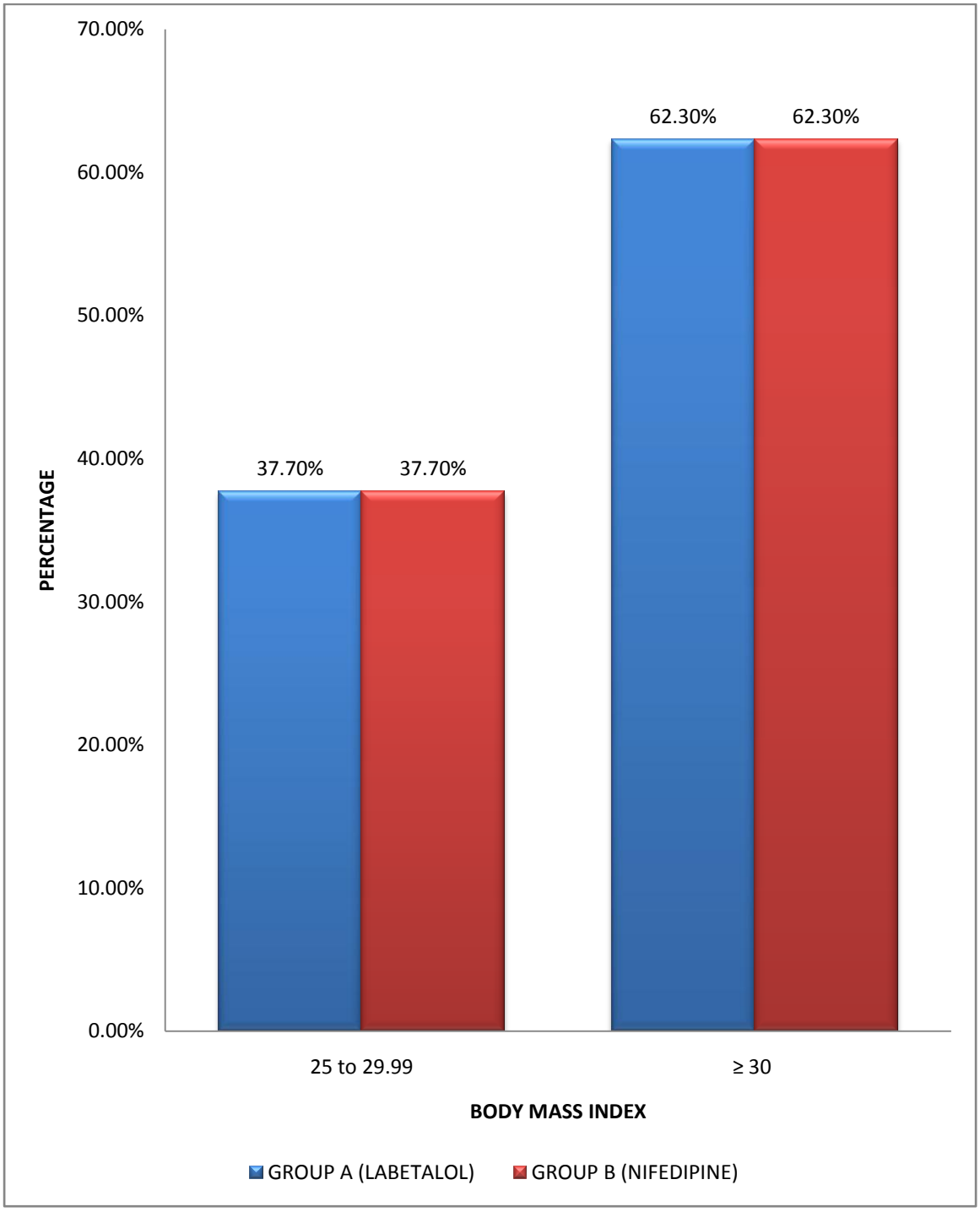


TABLE – 6

SYSTOLIC BLOOD PRESSURE

S. NO.	SYSTOLIC BLOOD PRESSURE	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	160 to 169 mm Hg	23	43.40%	19	35.80%	42 (39.6%)
2.	170 to 179 mm Hg	17	32.10%	28	52.80%	45 (42.5%)
3.	≥ 180 mm Hg	13	24.50%	6	11.20%	19 (17.9%)
MEAN (S.D.)		171 (9)		170 (8)		
STATISTICAL INFERENCE		T= 0.477 Degree of freedom = 104 0.635 > 0.05 Not Significant				

The baseline systolic blood pressure of the patients recruited in both the groups did not differ significantly. The mean systolic blood pressure in intravenous labetalol group was 171 mm Hg whereas it was 170 mm Hg in oral nifedipine group. 43.40% of patients in group A had a blood pressure range of 160 to 169 mm Hg. 52.80% of patients in nifedipine group had a blood pressure range of 170 to 179 mm Hg.

FIGURE – 6 A

SYSTOLIC BLOOD PRESSURE

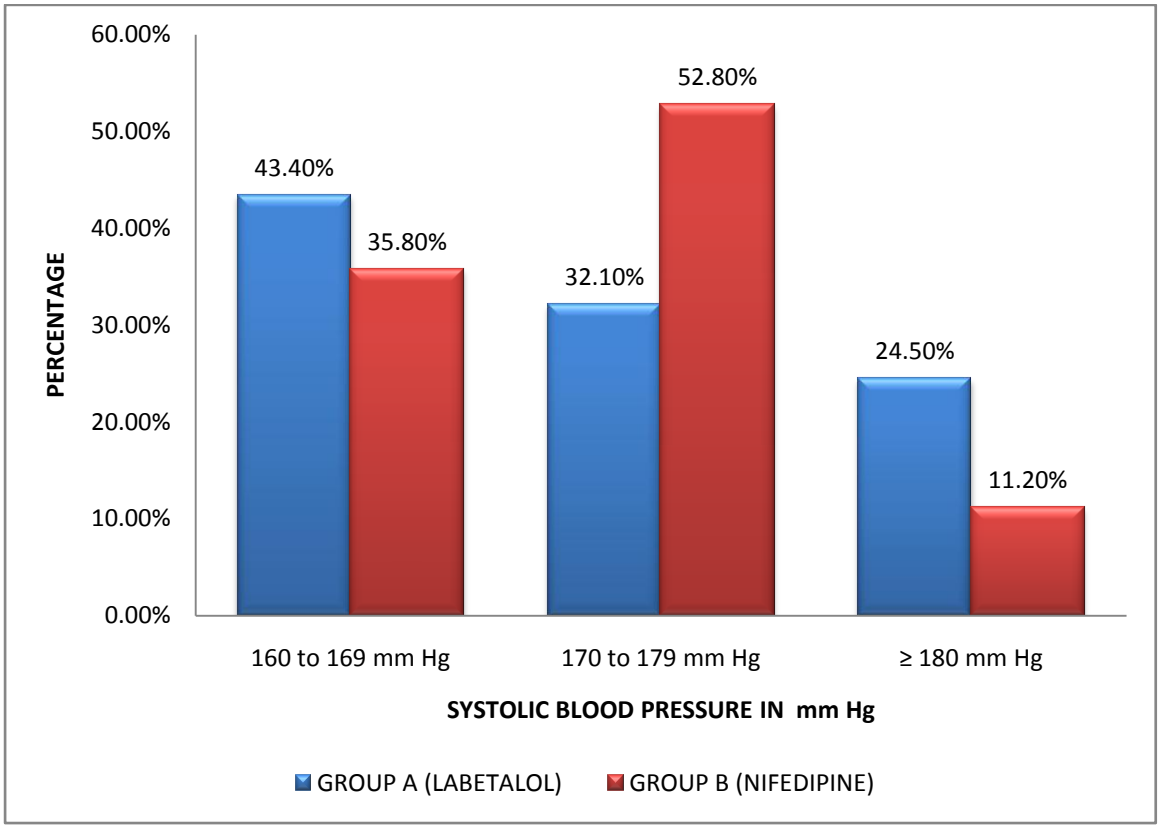


FIGURE – 6 B

SYSTOLIC BLOOD PRESSURE OF ALL THE PATIENTS

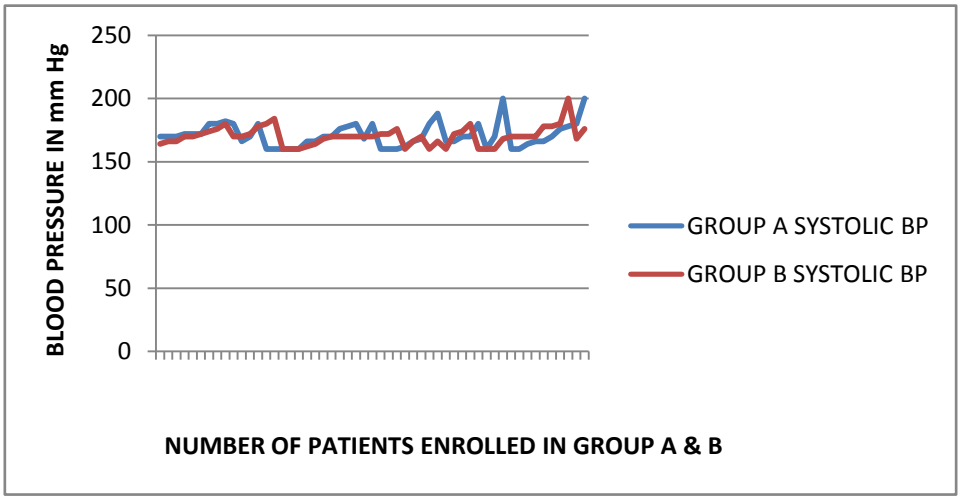


TABLE – 7

DIASTOLIC BLOOD PRESSURE

S. NO.	DIASTOLIC BLOOD PRESSURE	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	< 110 mm Hg	13	24.50%	15	28.30%	28(26.40%)
2.	≥ 110 mm Hg	40	75.50%	38	71.70%	78(73.60%)
MEAN (S.D.)		112(7)		111(8)		
STATISTICAL INFERENCE		T= 0.160 Degree of freedom = 104 0.873 > 0.05 Not Significant				

The baseline diastolic blood pressure did not vary significantly in the groups. The mean of the baseline diastolic blood pressure were 112 mm Hg and 111 mm Hg in the groups A and B, respectively. 75.50% and 71.70% in groups A and B had diastolic blood pressure more than 110 mm Hg.

FIGURE – 7 A

DIASTOLIC BLOOD PRESSURE

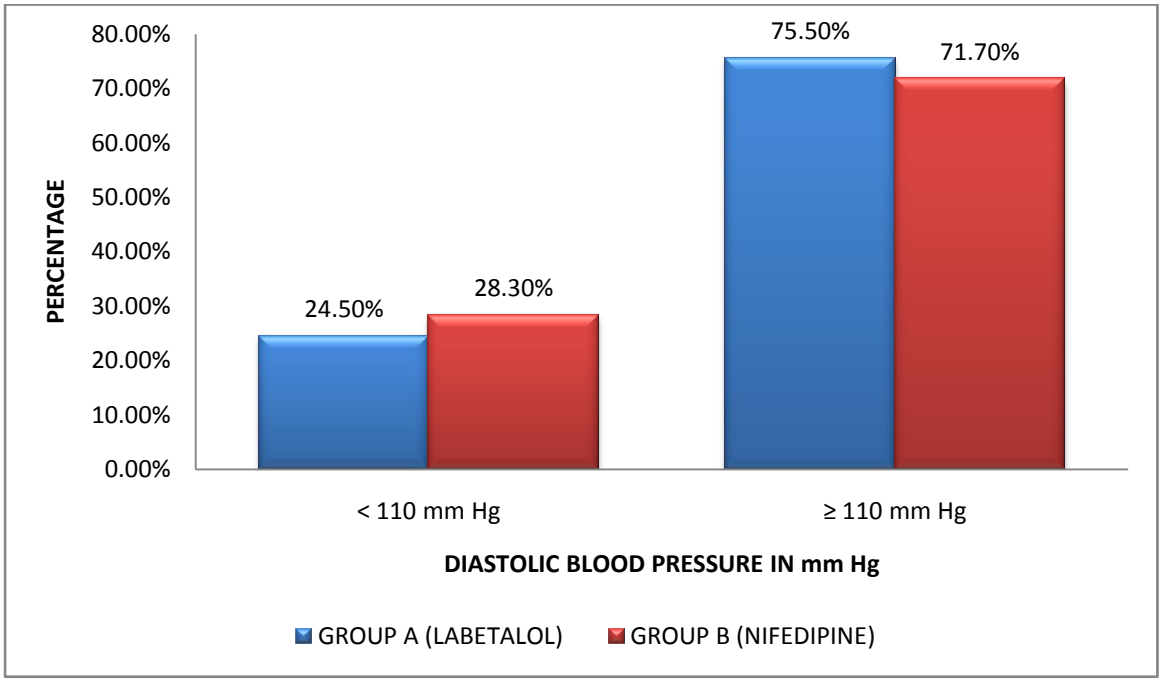


FIGURE – 7 B

DIASTOLIC BLOOD PRESSURE OF ALL THE PATIENTS

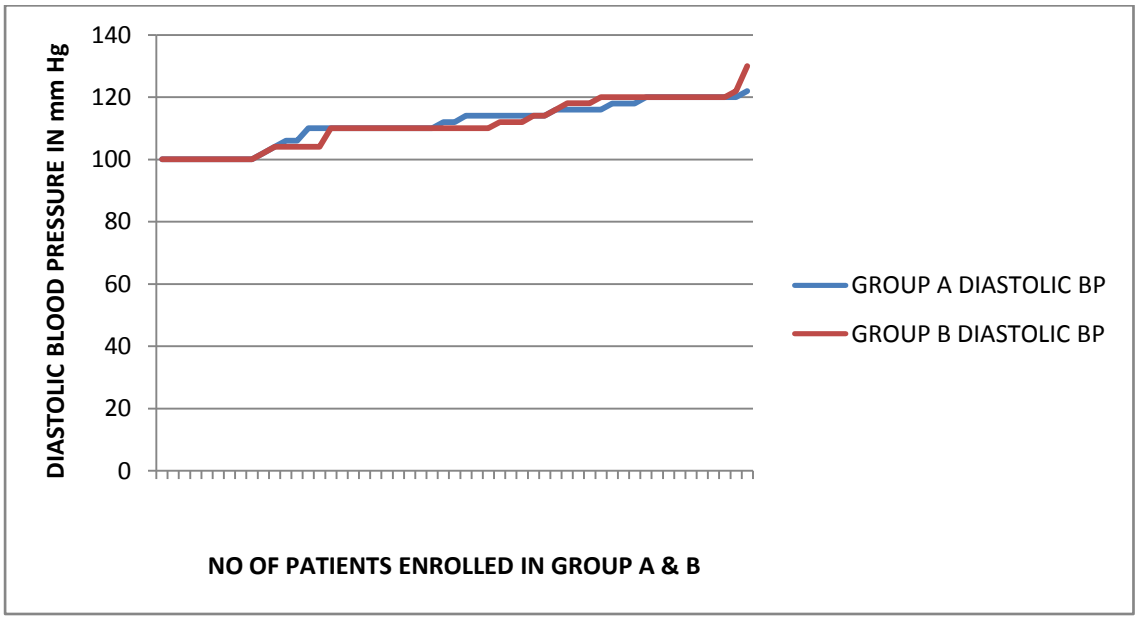


TABLE – 8

HEART RATE

S. NO.	HEART RATE	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	≤ 90 per minute	39	73.60%	44	83%	83(78.30%)
2.	91 to 100 per minute	12	22.60%	8	15.10%	20(18.90%)
3.	≥ 101 per minute	2	3.80%	1	1.90%	3(2.80%)
STATISTICAL INFERENCE		$\chi^2 = 1.435$ Degree of freedom = 2 0.488 > 0.05				

There was no significant difference in the baseline heart rate between the groups. Majority of the patients in group A (73.60%) and group B (83%) had heart rate less than 90 per minute during the commencement of the study.

TABLE – 9

DEGREE OF PROTEINURIA

S. NO.	PROTEINURIA	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	1+	21	39.62%	23	43.40%	44(41.50%)
2.	2+	13	24.53%	13	24.53%	26(24.50%)
3.	3+	19	35.85%	17	32.08%	36(34%)
STATISTICAL INFERENCE		$\chi^2 = 0.202$ Degree of freedom = 2 0.904 > 0.05				

Degree of proteinuria by dipstick estimation did not differ significantly in the groups A and B.

TABLE – 10

TIME TAKEN TO ACHIEVE TARGET BLOOD PRESSURE

S.NO.	TIME TAKEN	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)	
		NUMBER	%	NUMBER	%
1.	15 minutes	4	7.55%	1	1.89%
2.	30 minutes	8	15.09%	18	33.96%
3.	45 minutes	20	37.74%	12	22.64%
4.	60 minutes	13	24.53%	9	16.98%
5.	75 minutes	3	5.66%	7	13.21%
6.	$\geq$ 90 minutes	5	9.43%	6	11.32%
STATISTICAL INFERENCE		$\chi^2 = 9.112$ Degree of freedom = 6 0.167 > 0.05 No significant difference			

In group A, 20 patients, constituting 37.7% of the recruited reached the target blood pressure of less than 150/ 100 mm Hg in 45 minutes. 18 patients, constituting 34% of group B achieved the target blood pressure range by 30 minutes. The median time taken in group A is 45 minutes and that of group B is 30 minutes. Overall, there is no

statistically significant change regarding the time taken to achieve the target blood pressure.

FIGURE – 8

TIME TAKEN TO ACHIEVE TARGET BLOOD PRESSURE

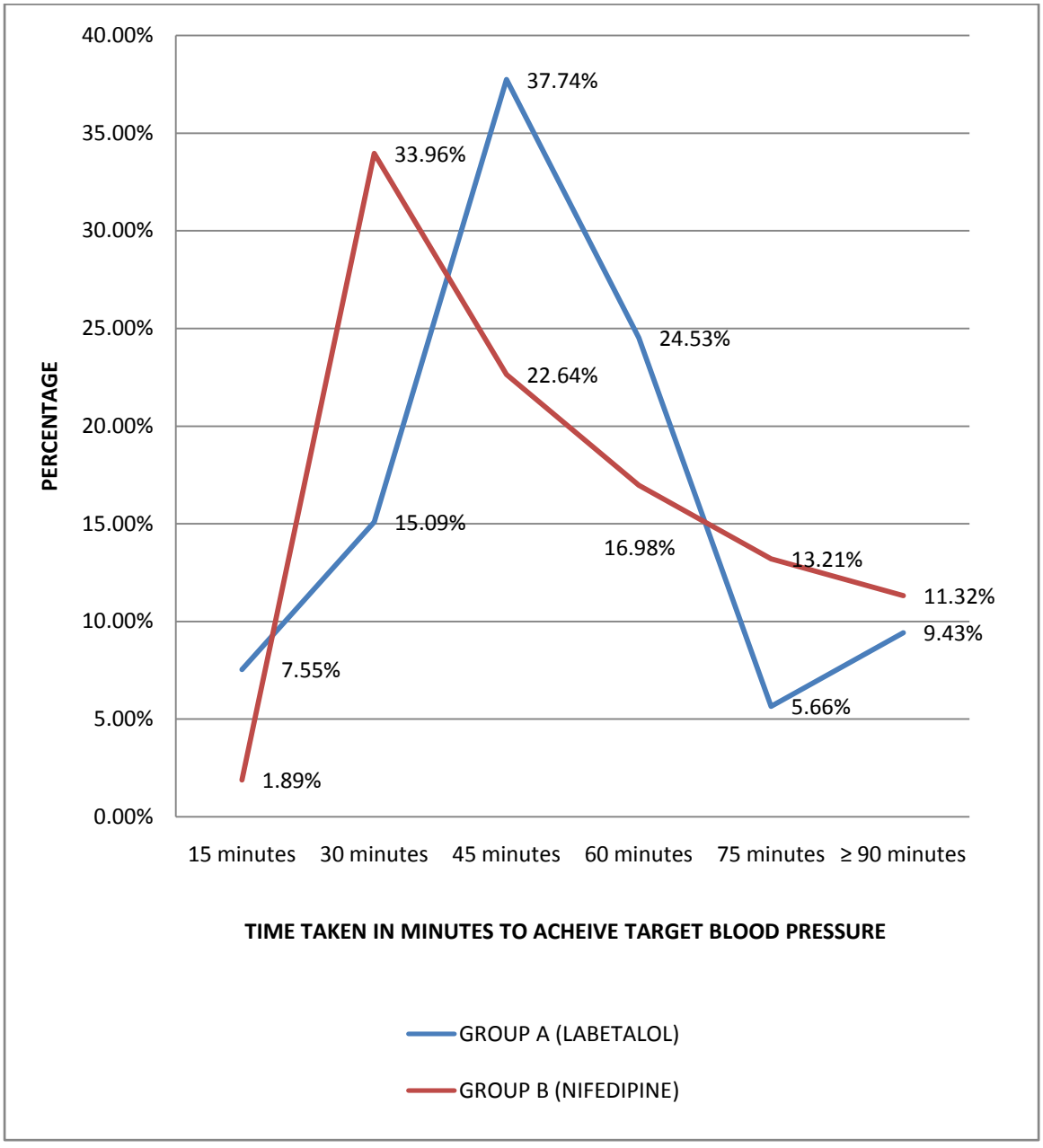


TABLE – 11

NUMBER OF DOSES REQUIRED TO ACHEIVE TARGET BLOOD PRESSURE

S. NO.	NUMBER OF DOSES	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	1	4	7.5%	1	1.9%	5 (4.72%)
2.	2	7	13.2%	18	34%	25 (23.58%)
3.	3	19	35.8%	14	26.4%	33 (31.13%)
4.	4	11	20.8%	9	17%	20 (18.87%)
5.	5	7	13.2%	5	9.4%	12 (11.32%)
6.	6	2	3.8%	2	3.8%	4 (3.77%)
7.	7	3	5.7%	4	7.5%	7 (6.60%)

STATISTICAL INFERENCE

$\chi^2 = 8.074$ Degree of freedom = 6

$0.233 > 0.05$

Not Significant

Excluding 5 patients in group A and 6 patients in group B, who required cross over treatment and achieved control of blood pressure at 105 minutes each, the rest of the patients (31.10%) reached target blood pressure of < 150/ 100 mm Hg after three

doses of antihypertensive. 35.80% of patients enrolled in group A reached the target blood pressure on administration of three consecutive doses of antihypertensive, while 34% of that in group B achieved target blood pressure in two doses of the drug administered. But the difference is not statistically significant.

FIGURE – 9

NUMBER OF DOSES REQUIRED TO ACHEIVE TARGET BLOOD PRESSURE

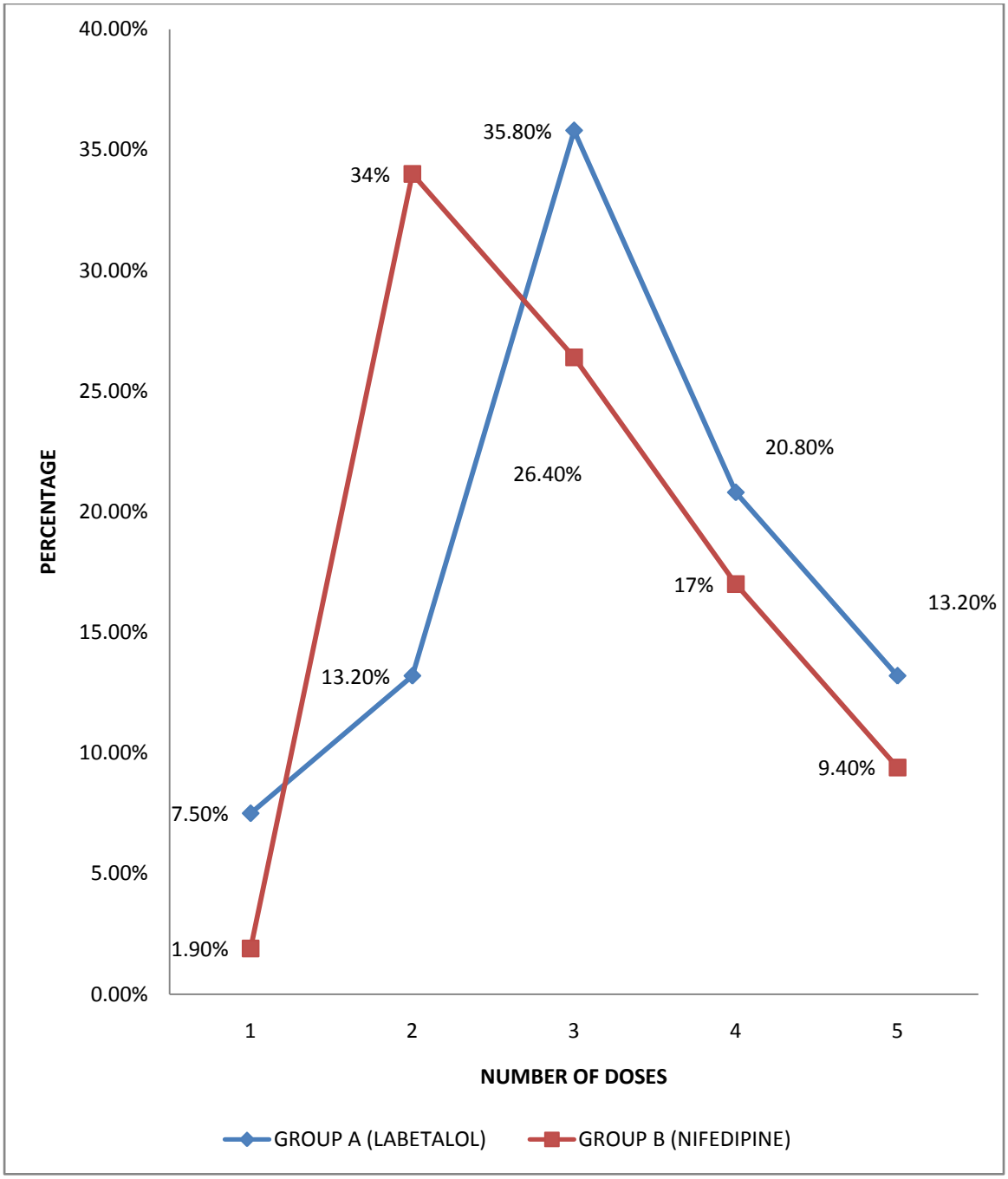

40.00%
35.00%
30.00%
25.00%
20.00%
15.00%
10.00%
5.00%
0.00%
PERCENTAGE
35.80%
34%
20.80%
26.40%
17%
13.20%
13.20%
9.40%
7.50%
1.90%
1
2
3
4
5
NUMBER OF DOSES
GROUP A (LABETALOL)
GROUP B (NIFEDIPINE)

TABLE – 12

SYSTOLIC BLOOD PRESSURE AFTER ANTI HYPERTENSIVE TREATMENT

S.NO.	SYSTOLIC BLOOD PRESSURE AT REGULAR TIME INTERVAL	GROUP A AND B	MEAN (S.D.)	STATISTICAL INFERENCE
1.	SYSTOLIC BP AT 15 MINUTES	LABETALOL (n=53)	166 (11)	T= 0.881 Df = 104 0.380 > 0.05 Not Significant
		NIFEDIPINE (n=53)	164 (8)	
2.	SYSTOLIC BP AT 30 MINUTES	LABETALOL (n=48)	162 (10)	T= 2.710 Df = 98 0.008 < 0.05 Significant
		NIFEDIPINE (n=52)	156 (11)	
3.	SYSTOLIC BP AT 45 MINUTES	LABETALOL (n=41)	155 (11)	T= -0.021 Df = 73 0.984 > 0.05 Not Significant
		NIFEDIPINE (n=34)	155 (11)	
4.	SYSTOLIC BP AT 60 MINUTES	LABETALOL (n=21)	153 (11)	T= -0.995 Df = 38 0.326 > 0.05 Not Significant
		NIFEDIPINE (n=19)	156 (10)	
5.	SYSTOLIC BP AT 75 MINUTES	LABETALOL (n=8)	156 (13)	T= 0.014 Df = 17 0.989 > 0.05 Not Significant
		NIFEDIPINE (n=11)	156 (8)	

The mean fall in systolic blood pressure in group A is the maximum at 45 minutes and that in group B is at 30 minutes. On comparison, the fall in systolic blood pressure

was significant at 30 minutes with a mean fall in group B of 156 mm Hg and that of group A was 162 mm Hg. The p value at 30 minutes is 0.008, which is significant.

FIGURE – 10 A

SYSTOLIC BLOOD PRESSURE AFTER ANTI HYPERTENSIVE TREATMENT

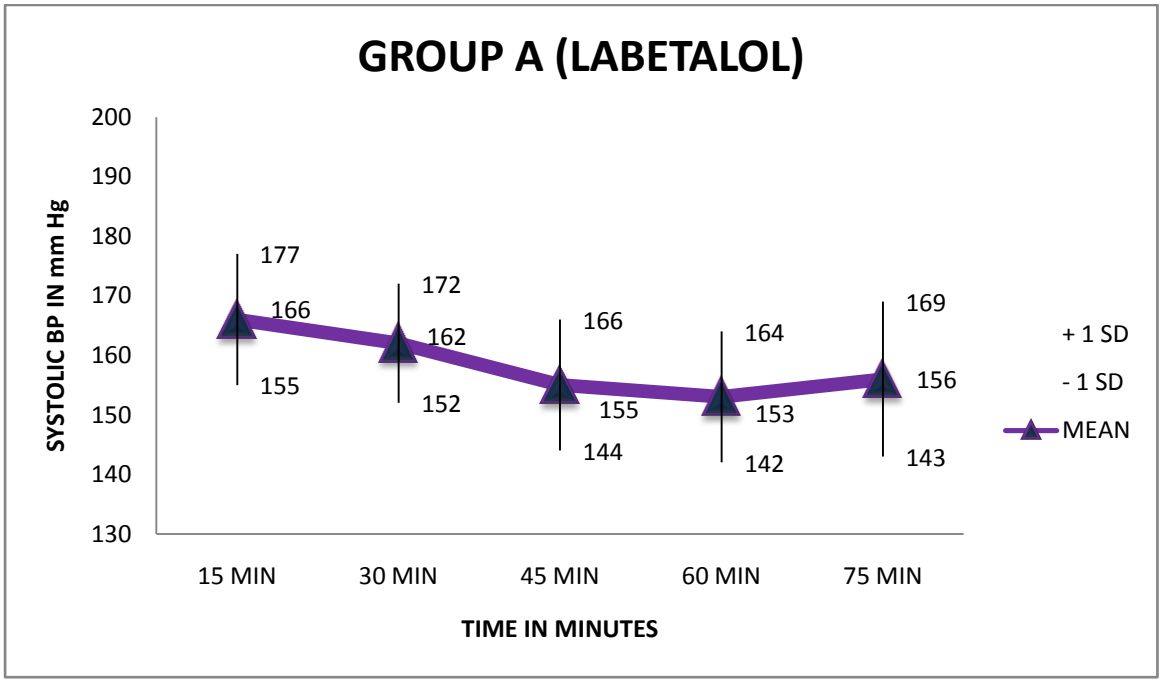


FIGURE – 10 B

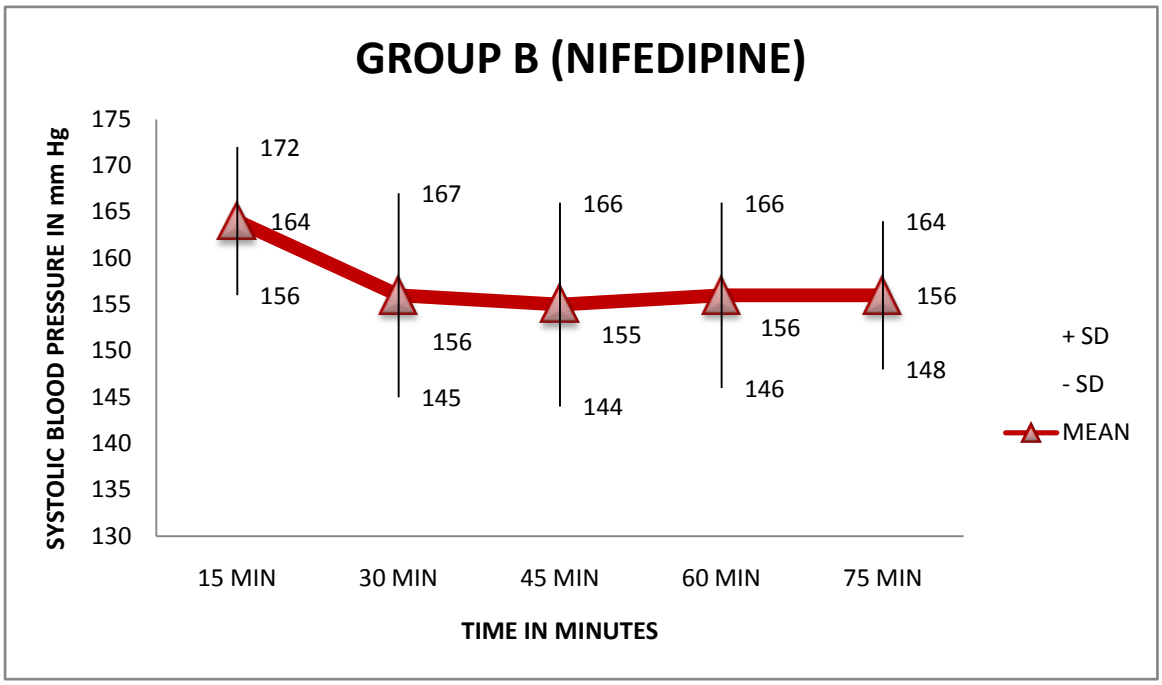


TABLE – 13

DIASTOLIC BLOOD PRESSURE AFTER ANTI HYPERTENSIVE TREATMENT

S.NO.	DIASTOLIC BLOOD PRESSURE AT REGULAR INTERVALS	GROUP A AND B	MEAN (S.D.)	STATISTICAL INFERENCE
1.	DIASTOLIC BP AT 15 MINUTES	LABETALOL *(n=53)*	106 (9)	T= -0.571 Df = 104 0.569 > 0.05
		NIFEDIPINE *(n=53)*	107 (8)	Not Significant
2.	DIASTOLIC BP AT 30 MINUTES	LABETALOL *(n=49)*	101 (10)	T= 0.371 Df = 99 0.711 > 0.05
		NIFEDIPINE *(n=52)*	100 (12)	Not Significant
3.	DIASTOLIC BP AT 45 MINUTES	LABETALOL *(n=41)*	96 (10)	T= -1.827 Df = 73 0.072 > 0.05
		NIFEDIPINE *(n=34)*	100 (10)	Not Significant
4.	DIASTOLIC BP AT 60 MINUTES	LABETALOL *(n=21)*	95 (7)	T= -1.134 Df = 39 0.264 > 0.05
		NIFEDIPINE *(n=20)*	98 (10)	Not Significant
5.	DIASTOLIC BP AT 75 MINUTES	LABETALOL *(n=8)*	96 (8)	T= -0.827 Df = 17 0.420 > 0.05
		NIFEDIPINE *(n=11)*	99 (9)	Not Significant

The fall in diastolic blood pressure was comparable in both the groups. The labetalol group has a greater mean fall of diastolic blood pressure at 45 minutes. The mean fall was greatest at 30 minutes for the nifedipine group. On comparison of both the

groups, the rate of fall of diastolic blood pressure was not found to be statistically significant.

FIGURE – 11 A

DIASTOLIC BLOOD PRESSURE AFTER ANTI HYPERTENSIVE TREATMENT

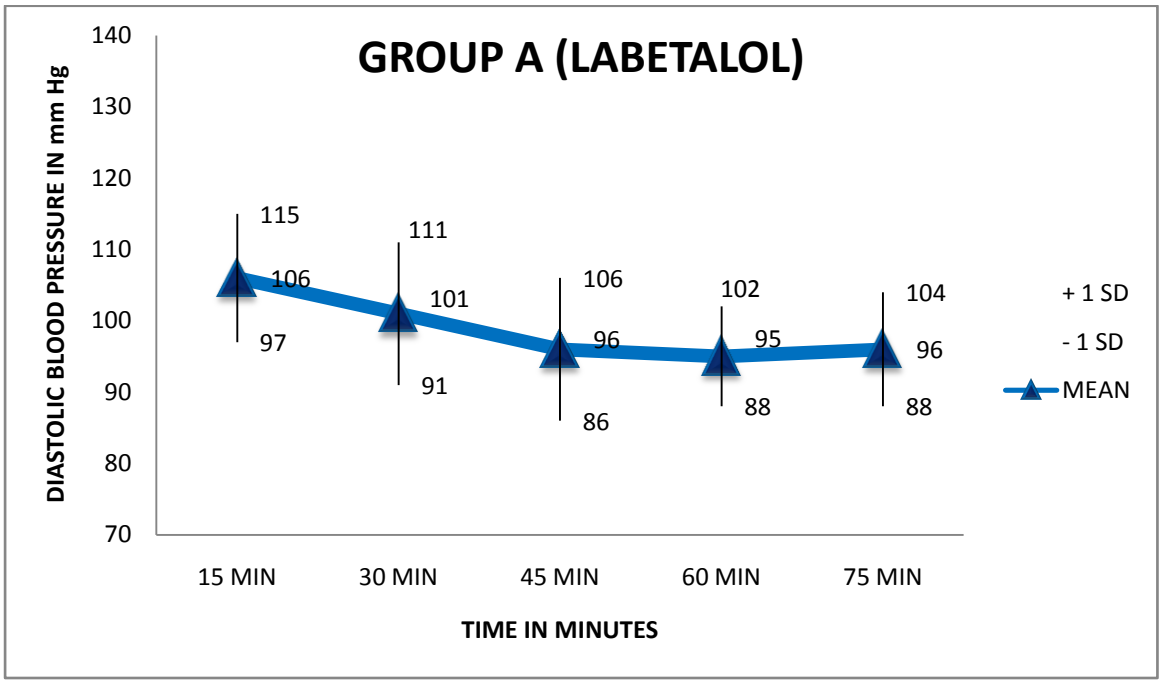


FIGURE – 11 B

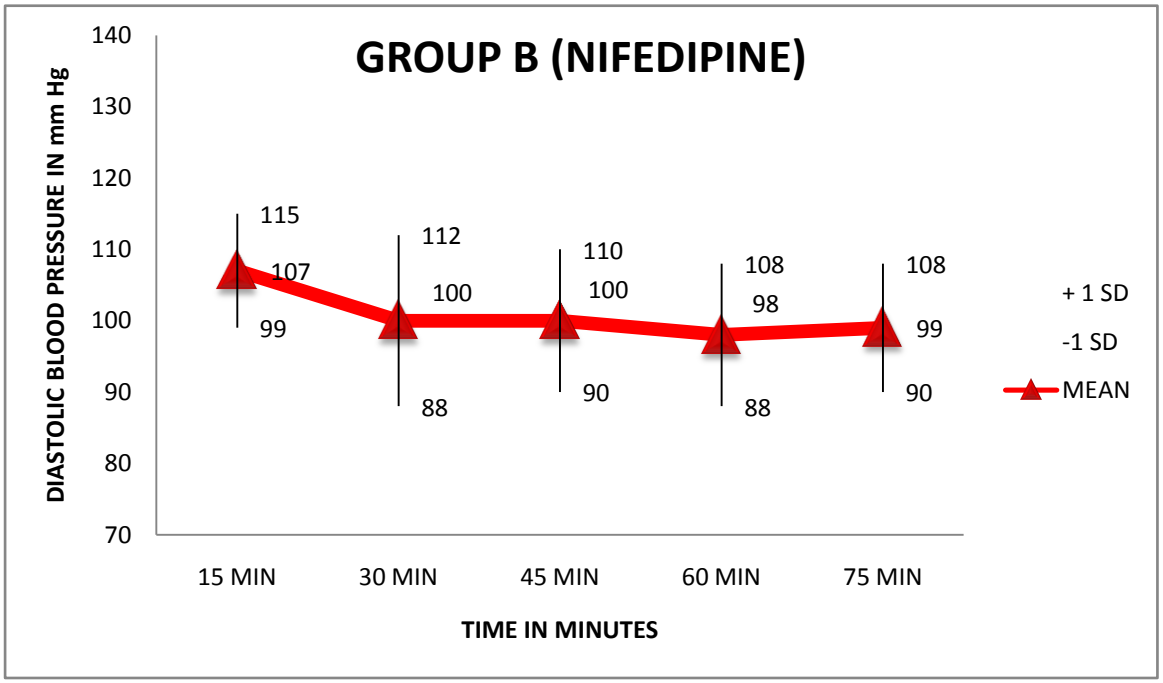


TABLE – 14

TREATMENT CROSS OVER

S. NO.	CROSS OVER	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	No	48	90.60%	47	88.70%	95(89.60%)
2.	Yes	5	9.40%	6	11.30%	11(10.40%)
STATISTICAL INFERENCE		χ^2= 0.101 Degree of freedom = 1 0.750 > 0.05 Not Significant				

Five patients (9%) out of 53 in group A and six patients (11%) in group B required cross over treatment to the alternate group. All the eleven patients from both the groups achieved control of blood pressure within 105 minutes of the commencement of the study.

FIGURE – 12

TREATMENT CROSS OVER

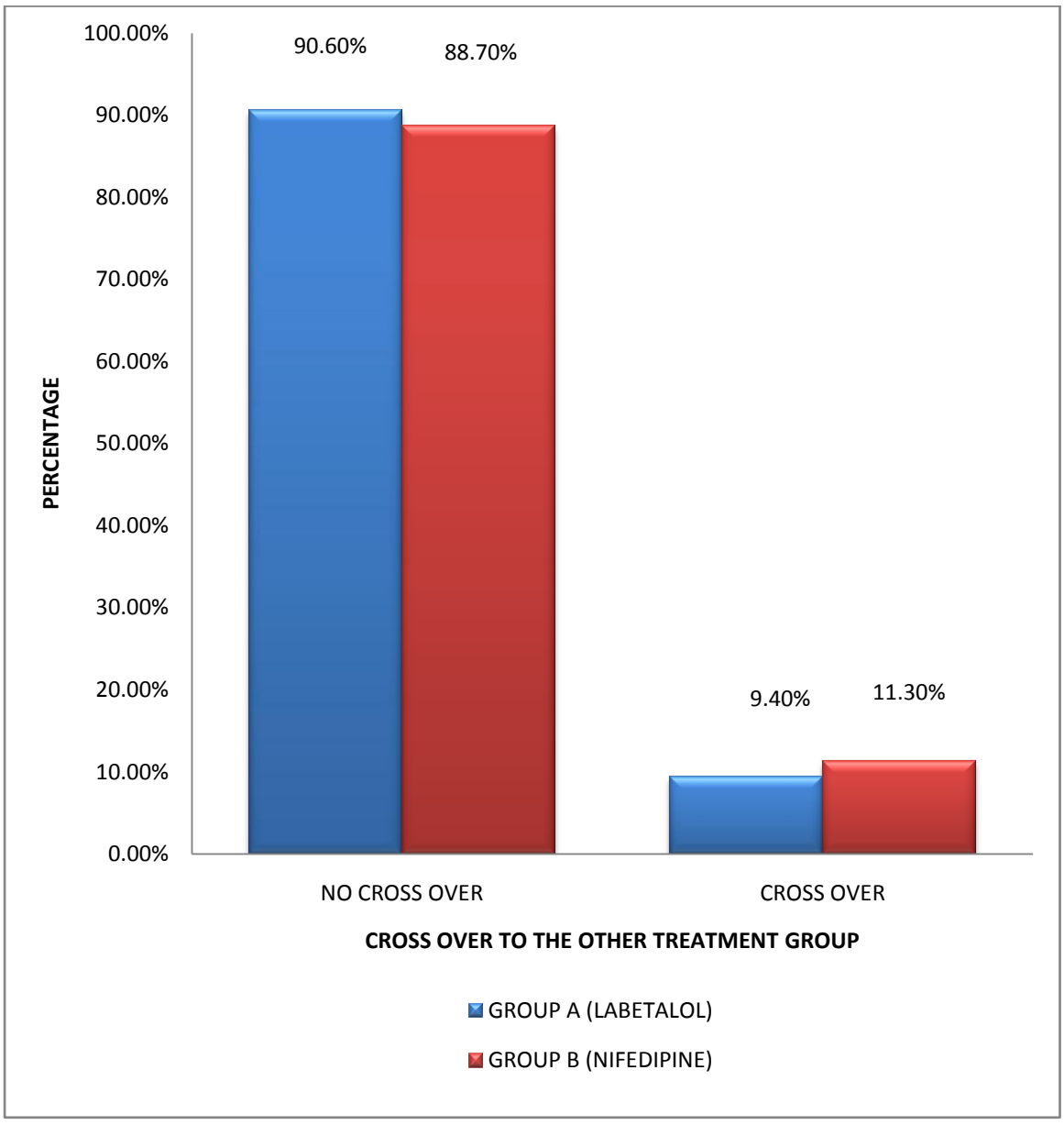


TABLE – 16

HEART RATE

S. NO.	HEART RATE AT REGULAR INTERVALS	GROUPS A AND B	MEAN (S.D.)	STATISTICAL INFERENCE
1.	HEART RATE AT 15 MINUTES	LABETALOL (n=53)	86(10)	T= 1.104 Df = 104
		NIFEDIPINE (n=53)	84(9)	0.272 > 0.05 Not Significant
2.	HEART RATE AT 30 MINUTES	LABETALOL (n=49)	85(9)	T= -2.166 Df = 99
		NIFEDIPINE (n=52)	89(8)	.033 < 0.05 Significant
3.	HEART RATE AT 45 MINUTES	LABETALOL (n=42)	84(8)	T= -5.653 Df = 75
		NIFEDEIPINE (n=35)	93(5)	.000 < 0.05 Significant
4.	HEART RATE AT 60 MINUTES	LABETALOL (n=23)	82(8)	T= -5.471 Df = 40
		NIFEDIPINE (n=19)	94(5)	.000 < 0.05 Significant
5.	HEART RATE AT 75 MINUTES	LABETALOL (n=13)	81(8)	T= -4.594 Df = 22
		NIFEDIPINE (n=11)	95(5)	.000 < 0.05 Significant

The difference in heart rate between labetalol and nifedipine groups was significant from 30 minutes of the commencement of the study. Patients in labetalol group had a progressive reduction in heart rate and that in nifedipine group showed a progressive rise in the same.

FIGURE – 13 A

HEART RATE

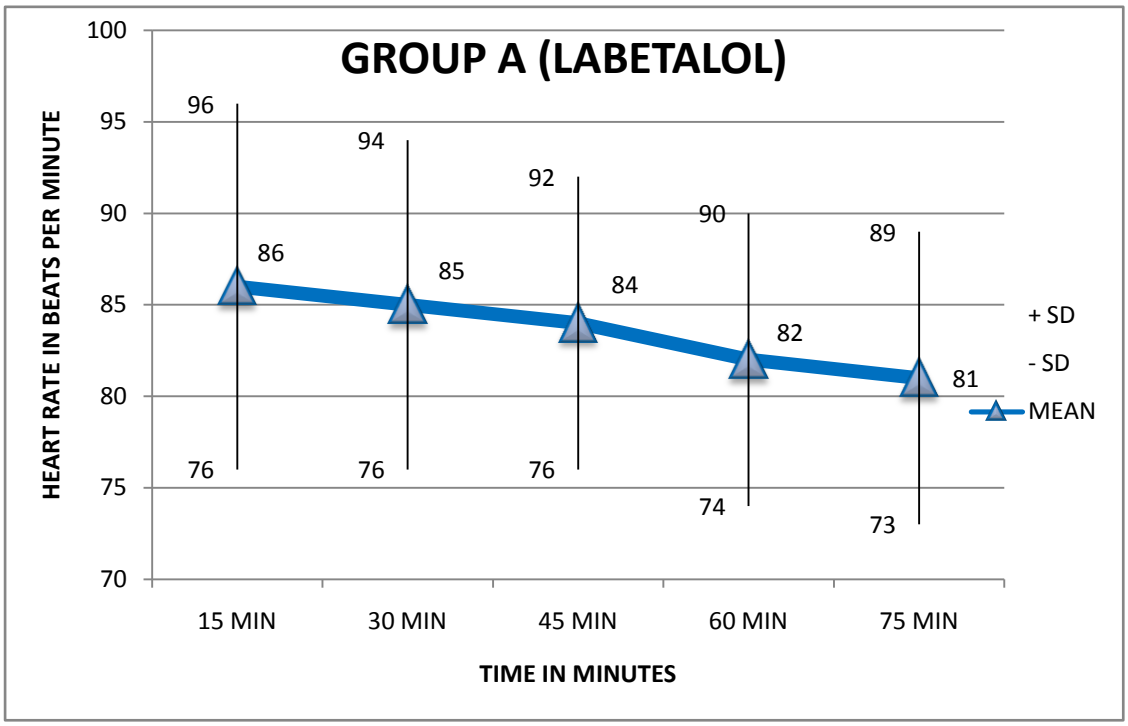


FIGURE – 13 B

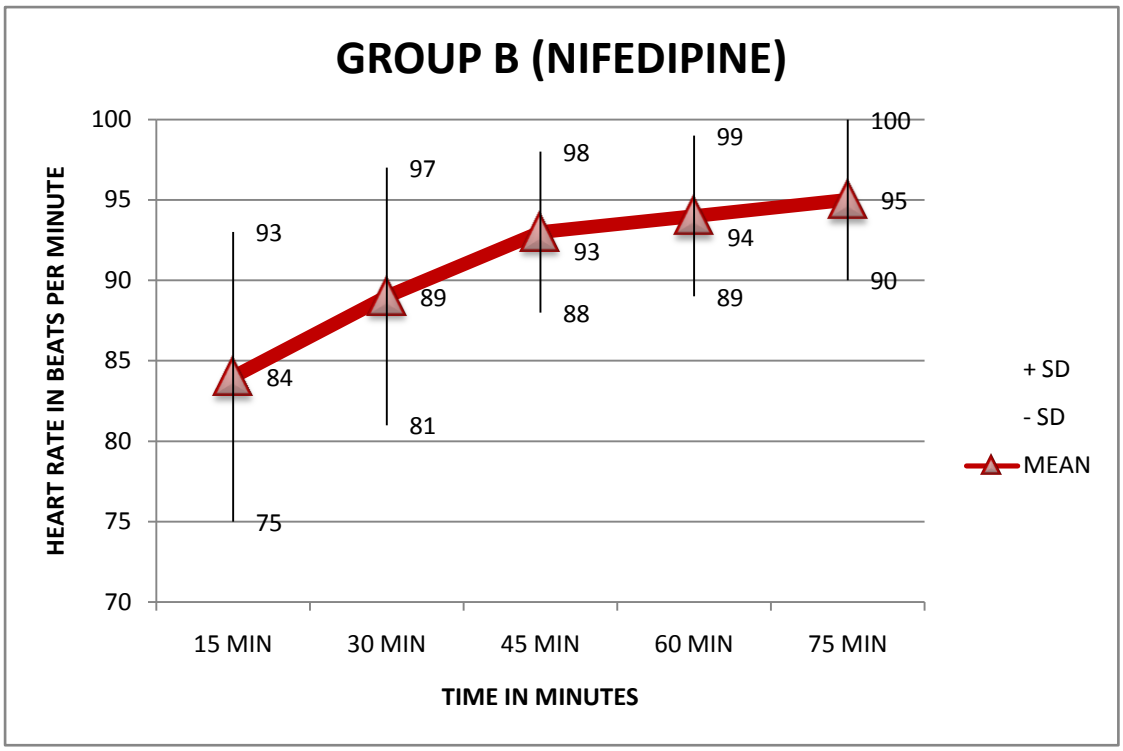


TABLE – 17

INDUCTION

S.NO.	INDUCTION	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	No induction	6	11.30%	3	5.70%	9(8.50%)
2.	Induction with cerviprime gel	47	88.70%	50	94.30%	97(91.50%)
STATISTICAL INFERENCE		χ^2=1.093 Degree of freedom = 1 0.296 > 0.05 Not Significant				

Delivery of the baby was expedited after control of blood pressure. Induction with cerviprime gel was done to 88.70% and 94.93% of patients in group A and B after stabilizing the blood pressure.

TABLE – 18

INDUCTION DELIVERY INTERVAL

S. NO.	INDUCTION DELIVERY INTERVAL	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)	
		NUMBER	%	NUMBER	%
1.	Less than 12 hrs	37	69.80%	34	64.20%
2.	More than 12 hrs	16	30.20%	19	35.80%
MEAN (S.D.)		13 (11)		13(11)	
STATISTICAL INFERENCE		T = -0.274 Degree of freedom = 104 0.785 > 0.05 Not Significant			

91.20% of the recruited patients were induced. 64.20% of the patients delivered within 12 hours of admission. There was no statistically significant variation in the groups A and B.

FIGURE – 14

INDUCTION DELIVERY INTERVAL

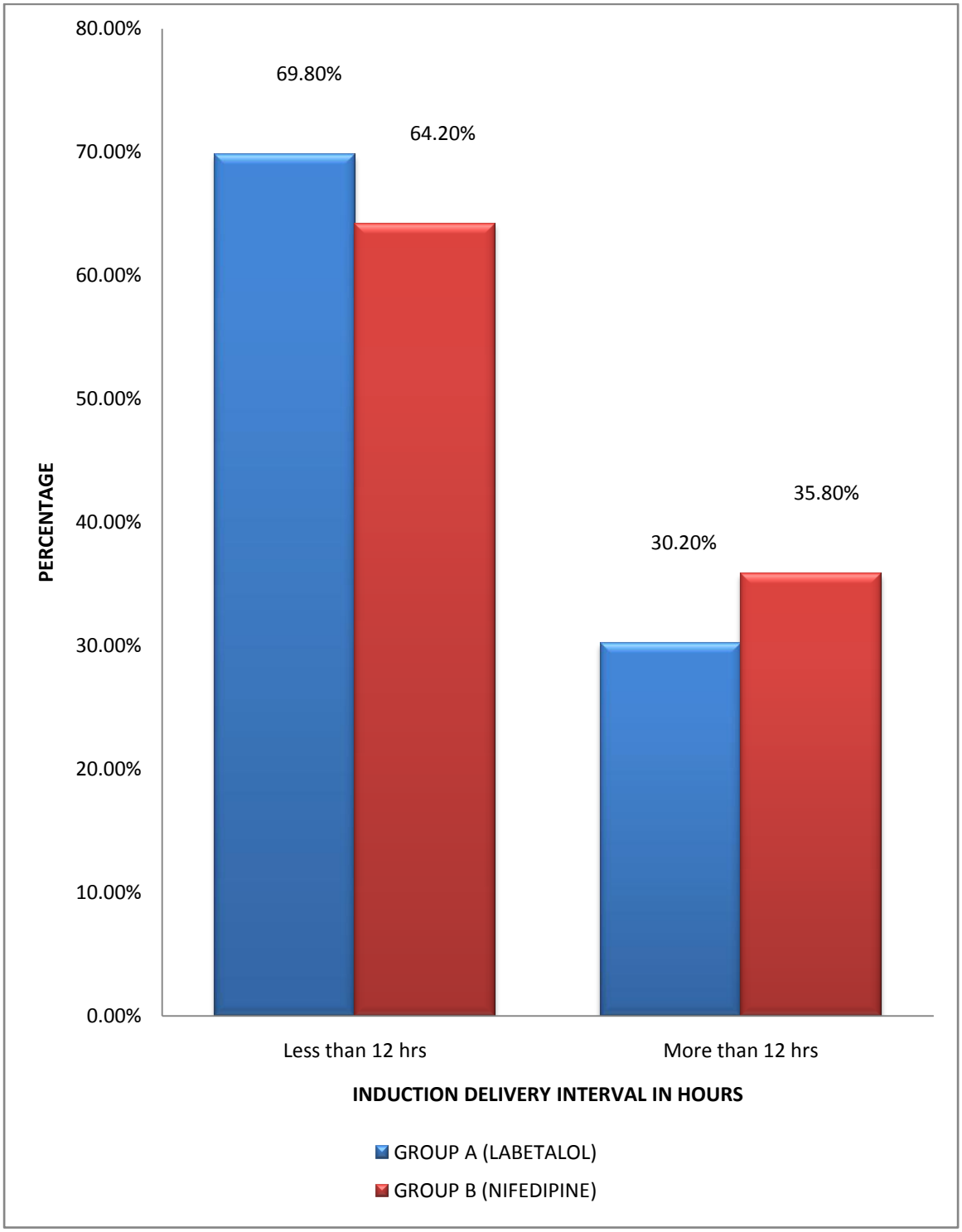


TABLE – 19

MODE OF DELIVERY

S. NO.	MODE OF DELIVERY	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		Total (n=106)
		NUMBER	%	NUMBER	%	
1.	Labour naturale	35	66%	39	73.60%	74(69.80%)
2.	LSCS	18	34%	14	26.40%	32(30.20%)
STATISTICAL INFERENCE		$\chi^2 = 0.716$ Degree of freedom = 1 0.397 > 0.05 Not Significant				

Caesarean section was done for obstetric indications. 74 patients, comprising 66% of group A and 73.6% of group B delivered vaginally. There were no cases of instrumental delivery in both the groups. Rest of the patients ended up in caesarean section. The outcome did not differ significantly in both the groups.

FIGURE – 15

MODE OF DELIVERY

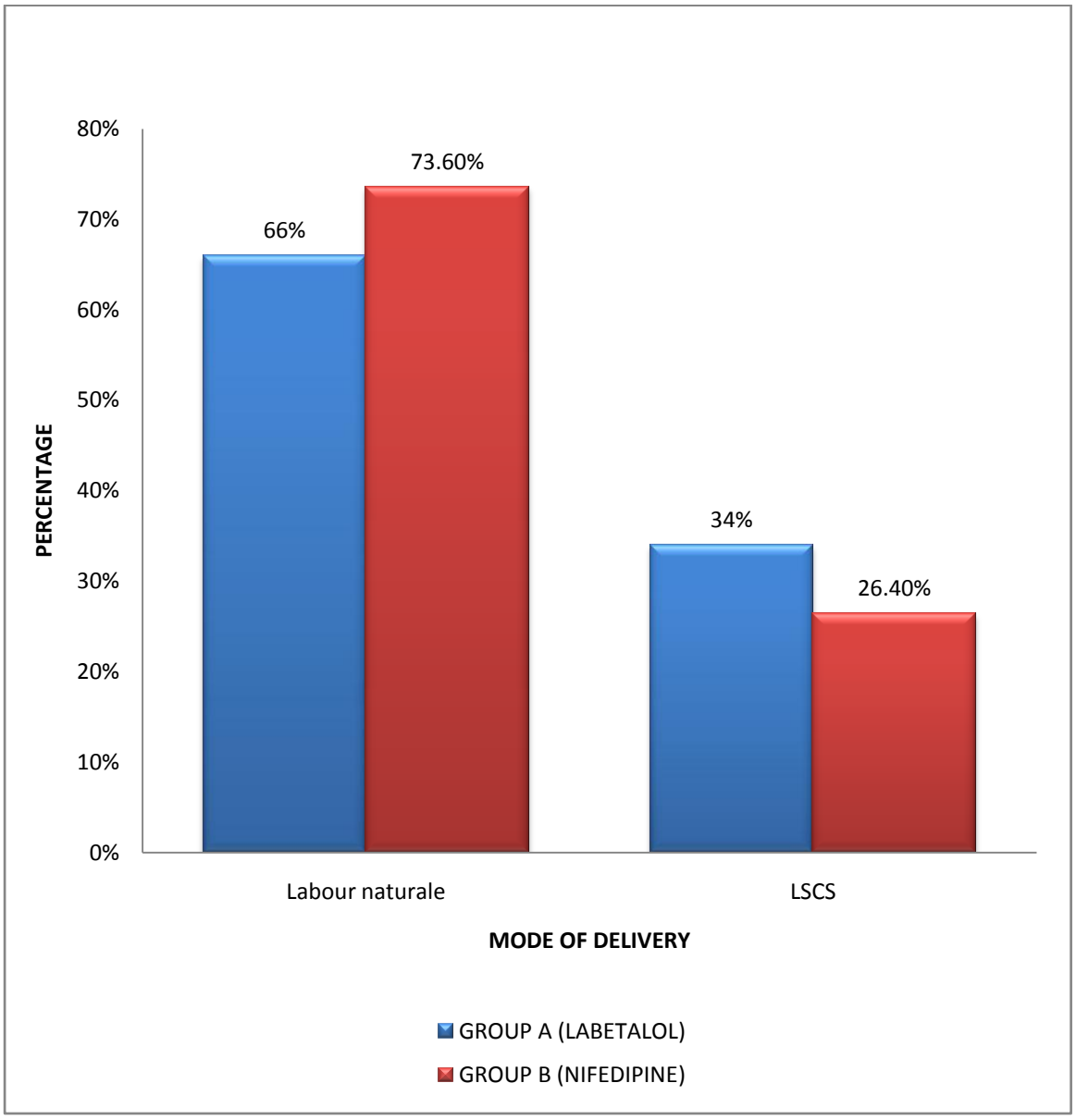


TABLE – 20

BIRTH WEIGHT OF THE BABY

S. NO.	BIRTH WEIGHT OF THE NEWBORN	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	1.5 to 1.9 kg	7	13.20%	9	17%	16(15.10%)
2.	2 to 2.4 kg	25	47.20%	24	45.30%	49(46.20%)
3.	2.5 kg & above	21	39.60%	20	37.70%	41(38.70%)
STATISTICAL INFERENCE		χ^2 = 0.295 Degree of freedom = 2 0.863 > 0.05 Not Significant				

47.20% and 45.30% babies of group A and B respectively had their birth weights ranging from 2 to 2.4 kg. The gestational age at admission of the majority of the patients was around 34 to 36 weeks in both the groups, with only a small percentage having an early onset disease. There was no significant difference in the outcome based on weight of the baby.

FIGURE – 16

BIRTH WEIGHT OF THE NEWBORN

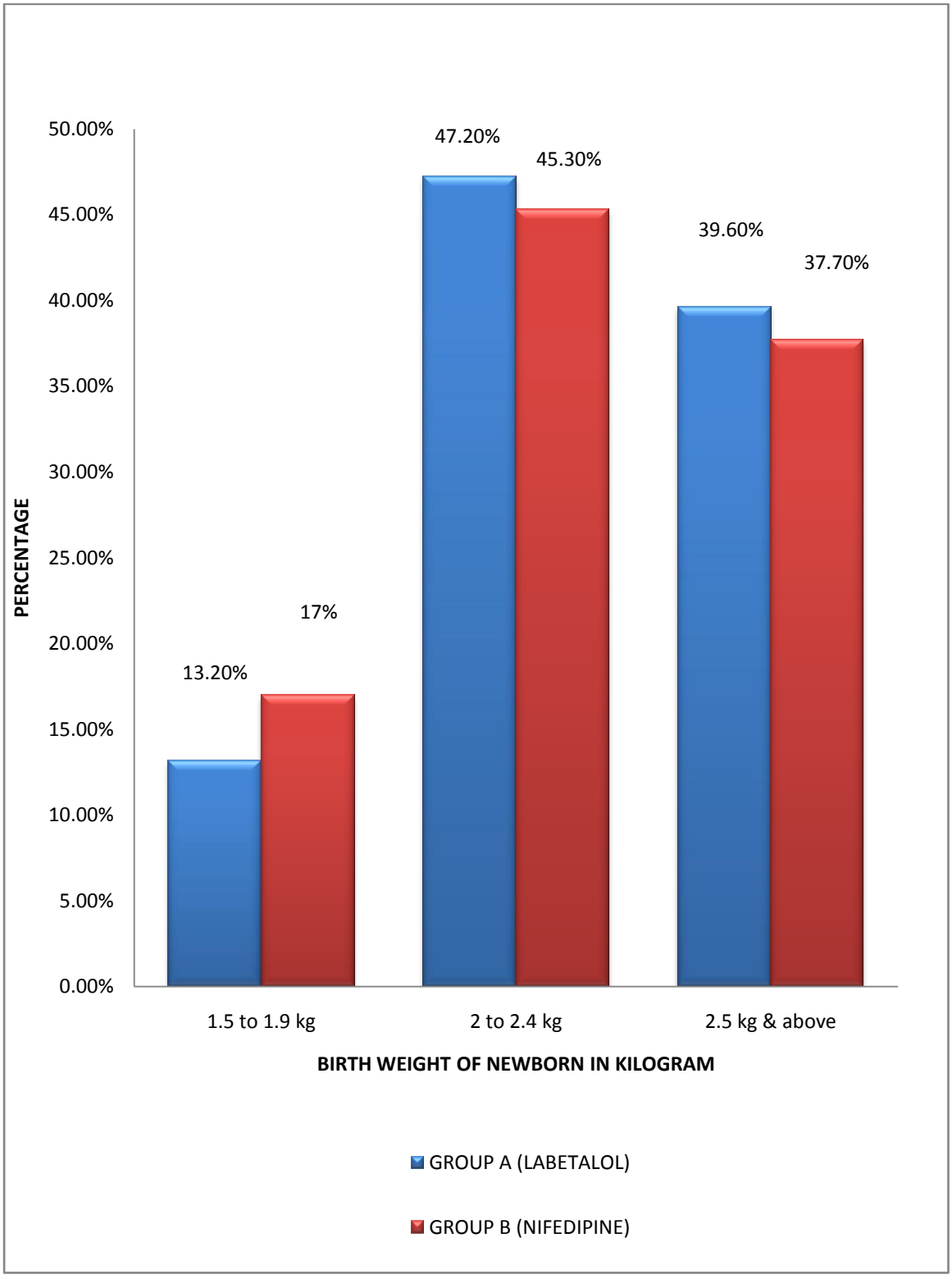


TABLE – 21

NEONATAL INTENSIVE CARE ADMISSIONS

S. NO.	NICU ADMISSIONS	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	No	46	86.80%	42	79.20%	88(83%)
2.	Yes	7	13.20%	11	20.80%	18(17%)
STATISTICAL INFERENCE		χ^2 = 1.071 Degree of freedom = 1 0.301 > 0.05 Not Significant				

The babies admitted to neonatal intensive care units were mostly due to the complications arising out of preterm labour. 17% of the enrolled mothers had their newborn admitted in intensive care unit. The difference did not vary significantly between the groups.

FIGURE – 17

NEONATAL INTENSIVE CARE ADMISSIONS

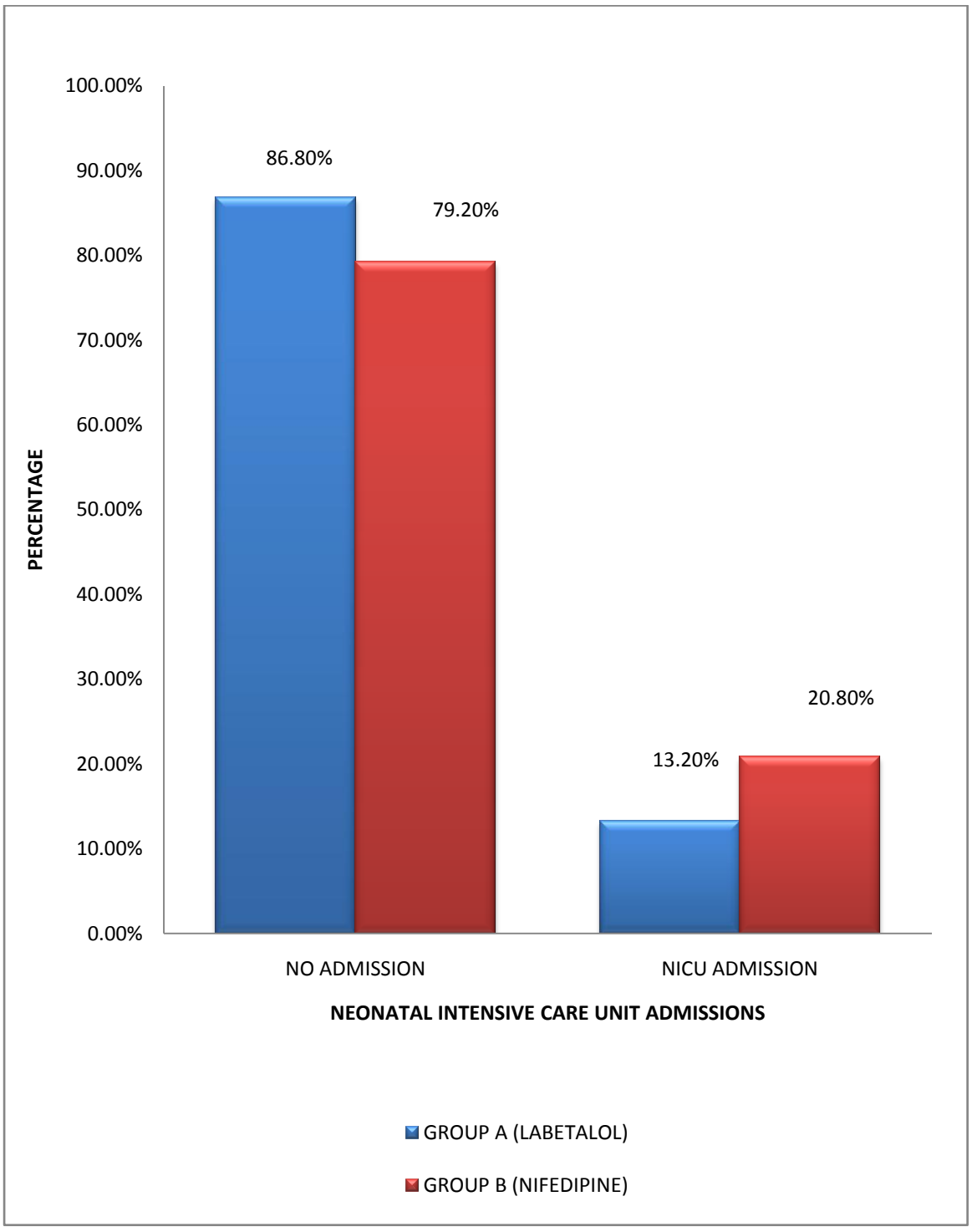


TABLE – 22

NEONATAL OUTCOME MEASURES

S. NO.	NEONATAL OUTCOME	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	Alive	49	92.50%	46	86.80%	95(89.6%)
2.	Dead	4	7.50%	7	13.20%	11(10.4%)
STATISTICAL INFERENCE		χ^2= 0.913 Degree of freedom = 1 0.339 > 0.05 Not Significant				

Neonatal outcome was accounted on discharge of the mother. Out of 17% of intensive care admissions, 11% of the babies died. The major cause was from neonatal respiratory distress syndrome arising out of prematurity. Approximately 15% of the patients enrolled in the study had gestational age less than 28 weeks. There was no significant change in terms of perinatal death in both the groups.

FIGURE – 18

NEONATAL OUTCOME MEASURES

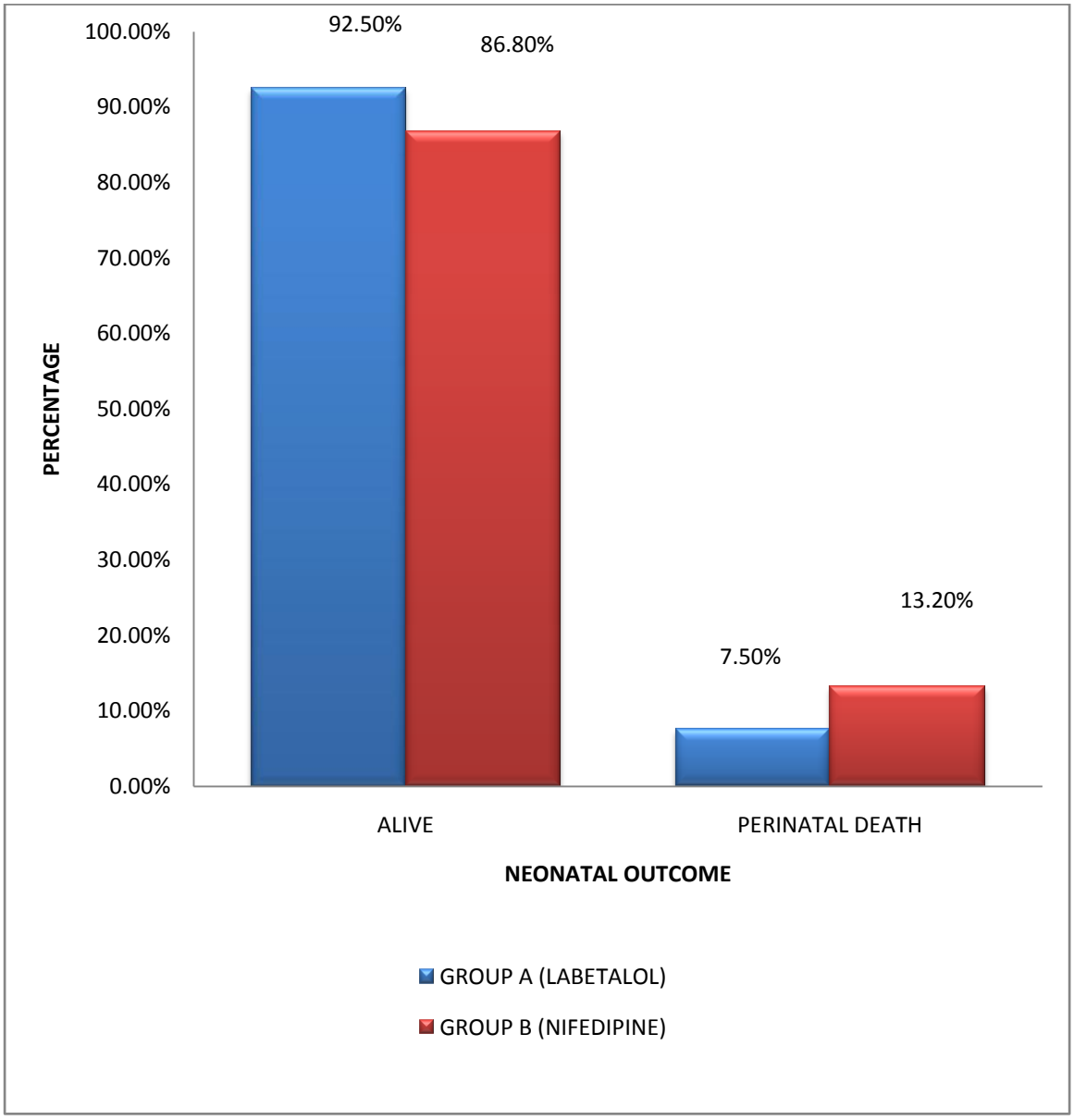


TABLE – 23

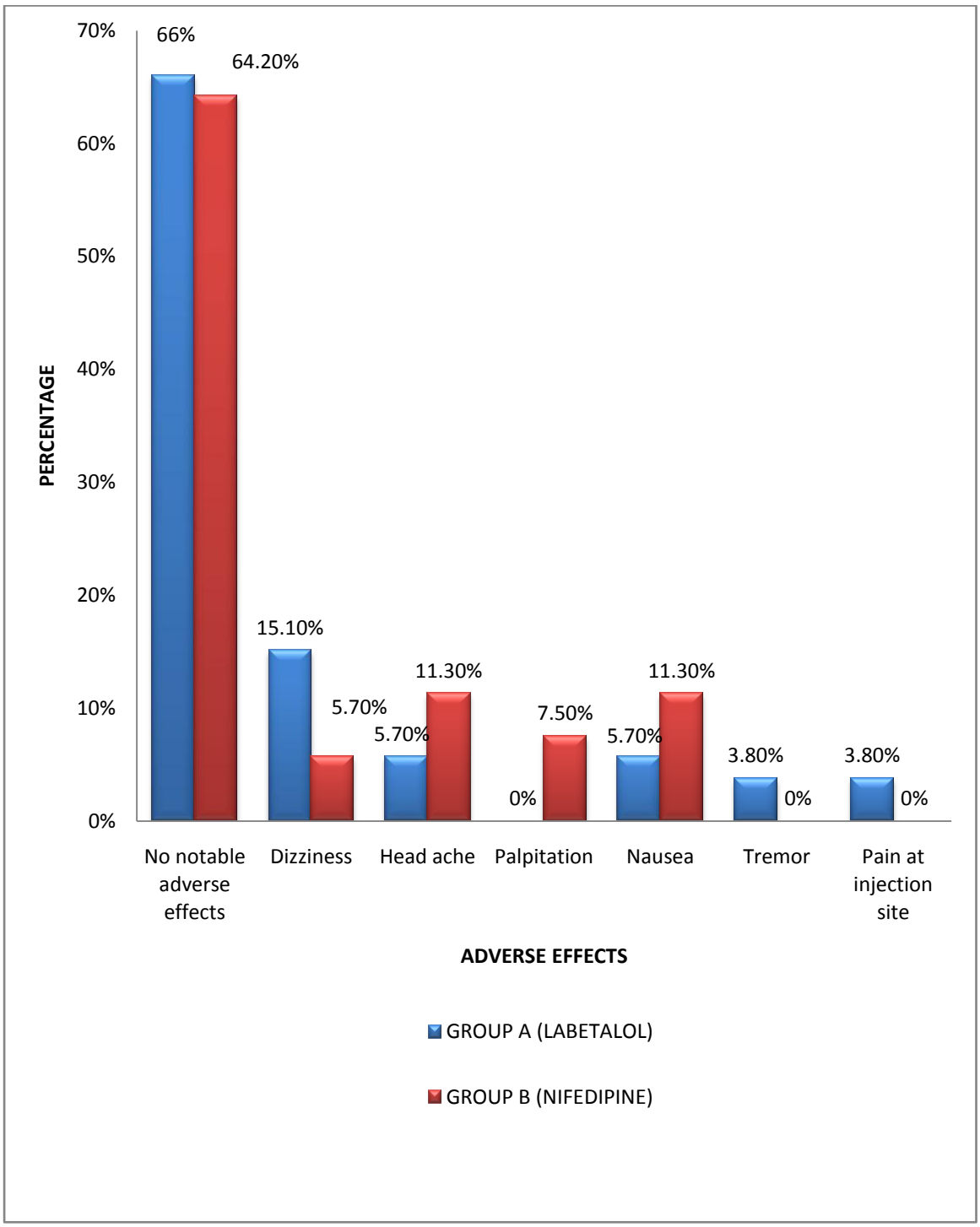
ADVERSE EFFECTS

S.NO.	ADVERSE DRUG REACTIONS	GROUP A LABETALOL (n=53)		GROUP B NIFEDIPINE (n=53)		TOTAL (n=106)
		NUMBER	%	NUMBER	%	
1.	No notable adverse effects	35	66%	34	64.2%	69 (65.1%)
2.	Dizziness	8	15.1%	3	5.7%	11 (10.4%)
3.	Head ache	3	5.7%	6	11.3%	9 (8.5%)
4.	Palpitation	0	0%	4	7.5%	4 (3.8%)
5.	Nausea	3	5.7%	6	11.3%	9 (8.5%)
6.	Tremor	2	3.8%	0	0%	2 (1.9%)
7.	Pain at injection site	2	3.8%	0	0%	2 (1.9%)
STATISTICAL INFERENCE		$\chi^2 = 12.287$ Degree of freedom = 6 0.056 > 0.05 Not Significant				

No notable adverse effects were reported in the majority of the recruited patients. In group A, the common adverse effects were dizziness (15.10%) and head ache and nausea (5.7%). There were no instances of palpitations in group A. The common adverse effect of patients recruited in group B was head ache (11.3%). Similar number also complained of nausea in group B. 7.5% and 5.7% of patients in group B complained of palpitations and dizziness respectively. Overall, there was no significant difference in adverse effects in both the groups.

FIGURE – 19

ADVERSE EFFECTS



DISCUSSION

Hypertensive emergency in pregnancy is associated with a considerable morbidity and mortality in both maternal and neonatal populations. The primary aim is to reduce the dangerously elevated blood pressure and ameliorate the severity of the disease.

In the present study, intravenous labetalol was compared with oral nifedipine in terms of efficacy and safety. The maternal and fetal outcome measures and side effect profiles of the drugs were also studied.

The patients enrolled in both the groups were comparable in terms of age, parity, booking status, gestational age at admission and body mass index.

The mean age of the patients enrolled in the study was 24.89 years and 24.81 years in labetalol and nifedipine groups respectively.

According to the study by Duckitt et al, primiparity is one of the risk factors for preeclampsia [54]. In the present study, 75.47% of labetalol group and 50.94% of nifedipine group were primigravida.

In the present study 40.57% patients presented in the gestational age of 34 to 36 weeks. Early onset disease at gestational age of less than 24 weeks was seen in 2.83% of the enrolled patients.

The progressive risk of preeclampsia in obese is elucidated in the study by Sibai and colleagues [55]. The risk is said to be increased by 13.3% in women with body mass index more than 35 kg/m^2. 62.30% of the patients enrolled in the labetalol and nifedipine groups fell under the category of obesity.

All the patients enrolled in the study were homogenous in terms of protienuria. 39.62% of patients in labetalol group and 43.40% of the patients in nifedipine group had 1+ proteinuria on urine dipstick estimation which approximates to 30 mg/dl of

proteinuria. 34% of the enrolled patients had 3+ proteinuria which amounts to 1 to 2 g/day of protienuria.

In a randomized control trial conducted by Sibai, Brian, et al, on the expectant management of severe preeclampsia, the blood pressure on admission was found to be ≥160/110 mm Hg [19]. Naidu, et al conducted a prospective study based on the finding through radiological investigative modalities such as single photon emission and cerebral computerised tomographic scan (SPECT) and transcranial Doppler findings in patients with eclampsia. 75% of the patients had perfusion defects in the watershed area in the parieto-occipital lobe arising out of cerebral vasospasm [56]. The loss of cerebral autoregulation at elevated blood pressures, more particularly at a systolic blood pressure of more than 160 mm Hg, was theorized by Schwartz and co-workers in 2000 [57].

The mean systolic blood pressure of the patients enrolled in the labetalol and nifedipine groups in the present study was 171 mm Hg and 170 mm Hg, respectively. The mean diastolic blood pressure was 112 and 111 mm Hg in labetalol and nifedipine groups, respectively.

According to the Cochrane database on review of drugs, the utility of the antihypertensive drug should be based on the experience of the clinician with respect to its utility and adverse effects. [4]

In a double blind randomized trial by Raheem et al [58], it was shown that both labetalol and nifedipine are equally efficacious in controlling blood pressure. The reduction in systolic and diastolic blood pressure was comparable in both the groups. 20% of the enrolled patients required cross-over treatment, in his trial.

A similar study conducted by Vermilion [59] et al shows that oral nifedipine is superior when compared to labetalol in blood pressure control. The drug protocol used in the study differed from the present study. Vermilion used 20 mg oral nifedipine after the initial 10 mg dose.

In the present study, out of the 53 patients enrolled in labetalol group, 20 patients, constituting 37.74% of the study population achieved the target blood pressure of ≤ 150/100 mm Hg in 45 minutes of commencement of the treatment, requiring three incremental doses of intravenous labetalol. The total dose administered was in labetalol group was 140 mg.

In the nifedipine group, 33.96% of the enrolled patients required two doses of oral nifedipine constituting a dose of 20 mg of the drug. However, on statistical analysis, there was no significant difference in the time taken for both the drugs to act for reduction in systolic blood pressure. On the whole, except for the 11 patients who required cross over treatment, all the patients constituting 89.60% attained blood pressure control at 75 minutes.

On statistical analysis of the trend in reduction of the systolic blood pressure with respect to time, the difference of reduction in blood pressure was found to be significant at 30 minutes cut off. Oral nifedipine was found to be associated with a greater reduction in systolic blood pressure with respect to time. Similar trend was not seen in the case of reduction in diastolic blood pressure. Both the drugs were comparable in their reduction in diastolic blood pressure in the present study.

Eleven patients, five in labetalol group and six in nifedipine group, comprising 10.40% of the enrolled in the study, required cross over treatment. The number of doses of the other respective drugs after the crossover was similar in both the groups.

The above mentioned patients achieved blood pressure control at 105 minutes after the commencement of the study.

None of the enrolled patients developed hypotension during the study. The lowest blood pressure recorded during the study was 130/80 mm Hg.

All the patients enrolled in the study received prophylactic magnesium sulphate therapy. None of the patients developed eclampsia in ante partum or post partum periods. The Magpie trial [37] recruiting 10141 women with preeclampsia showed that there was no significant interaction of nifedipine and magnesium sulphate. Similarly, in the present study, none of the patients receiving both the drugs developed hypotension or neuromuscular blockade.

Sibai et al compared the maternal and neonatal outcomes in expectant versus aggressive management in severe preeclampsia in a specific set of population [19]. The study showed better neonatal outcomes in terms of gestational age at delivery, birth weight and intensive care.

Once the blood pressure was controlled, 97% of the enrolled patients in the present study were induced with cerviprime gel to expedite delivery. In patients with gestational age less than 34 weeks, steroids were administered after the control of blood pressure to accelerate the lung maturity. Fetal monitoring was done with non stress test before and after administration of anti hypertensive drugs and after induction of the patients. There was no cardiotocographic abnormality associated with the use of both the drugs.

Among the patients enrolled, 69.80% delivered vaginally and 30.20% delivered by caesarean section. 49.20% of the babies delivered had their birth weights ranging from 2 to 2.4 kg. In patients with early onset disease and those associated with intrauterine growth restriction, the birth weight was less than 1.9 kg which made

15.10% of the enrolled patients. There was no significant difference in birth weight in both the groups.

13.20% of new born from labetalol group and 20.80% of new born from nifedipine group were admitted for intensive care. The causes of admission were extreme prematurity and respiratory distress syndrome. The outcome was similar in both the groups. None of the newborn had neonatal hypoglycaemia or hypotension after birth.

Out of 17% of the newborn admitted for intensive care, 7.50% of newborn from labetalol group and 13.20% of newborn from nifedipine group died due to extreme prematurity.

Majority of the patients enrolled in the study did not report any notable adverse effects. The most commonly reported adverse effect in labetalol group was dizziness and that in nifedipine group was head ache and nausea. None of the patients in the labetalol group had palpitations, though 7.5% of patients in the nifedipine group had complained of the same. 3.8% of the patients enrolled in the labetalol group had complained of tremor and pain at the injection site. On the whole, there was no statistically significant difference in adverse effects between both the groups.

The present study has certain limitations. The blood pressure and drug titration after the initial control of hypertension was not taken into account in the study. None of the patients with severe preeclampsia were managed expectantly because of the institutional protocol.

SUMMARY

- In the present study, out of the 106 antenatal patients with sustained severe hypertension, 53 were randomized to receive intravenous labetalol treatment and the rest were randomized to oral nifedipine treatment and the two groups were compared in terms of efficacy and safety of the treatment, adverse effects and maternal and perinatal outcome measures.
- All the patients recriuited in the study achieved blood pressure control. Majority of the patients in labetalol group (37.74%) achieved target blood pressure at 45 minutes and that with the nifedipine group (33.96%) achieved the target blood pressure at 30 minutes.
- 25.80% in labetalol group received three doses of the drug. 26.40% of the patients received two doses of the drug in nifedipine group.
- The rate of fall of blood pressure was the highest at 45 minutes for labetalol group and at 30 minutes for the nifedipine group.
- 10.40% of the patients required more than five doses and the treatment was crossed over to the other respective groups. All the patients in the cross over group achieved target blood pressure within 105 minutes.
- None of the patients had hypotensive episodes. There were no instances of fetal cardiotocographic abnormalities during the trial period.
- Both the groups exhibited significant differences in heart rate after 30 minutes of the commencement of the treatment. The heart rate declined with respect to time in the labetalol group. There was a rise in heart rate in the nifedipine group.

- 91.50% of the enrolled patients were induced to expedite delivery. 66% in labetalol group and 73.60% in nifedipine group delivered vaginally.
- There was no maternal mortality. All the patients were discharged without any residual complications. Perinatal mortality was 7.50% and 13.20% in labetalol and nifedipine group respectively.
- No notable adverse effect was reported by 65.10% of the patients. 15.10% of patients in labetalol group had dizziness. 11.3% of the patients in nifedipine group had headache and nausea.

CONCLUSION

Management of severe preeclampsia is in the control of blood pressure, prevention of complications, fetal surveillance and expedition of delivery if indicated. In the present study, the trend in reduction of blood pressure in patients with sustained severe hypertension with the use of intravenous labetalol and nifedipine was compared.

From the present study, both the drugs were found to be safe and effective in the reduction of blood pressure. None of the drugs were associated with any detrimental maternal or fetal outcomes with respect to the anti hypertensive usage. The tolerance of the patients towards both the drugs was similar.

Intravenous labetalol provided a smooth and steady reduction in blood pressure. The use of nifedipine may be recommended in low resource settings since it has an oral regimen and dosage is simple when compared to incremental intravenous dosing of labetalol.

In conclusion, both intravenous labetalol and oral nifedipine are equally efficacious and can be used as first line drugs for the use in acute blood pressure control of hypertensive emergency of pregnancy.

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PROFORMA

A RANDOMIZED TRIAL OF INTRAVENOUS LABETALOL VERSUS ORAL NIFEDIPINE IN ACUTE BLOOD PRESSURE CONTROL IN HYPERTENSIVE EMERGENCIES OF PREGNANCY

NAME: AGE: IP NO:

HUSBAND NAME: BOOKED/ UNBOOKED:

C/O:

MENSTRUAL HISTORY:

MARITAL HISTORY: OBSTETRIC HISTORY:

PAST SURGICAL HISTORY: PAST MEDICAL HISTORY:

FAMILY HISTORY: PERSONAL HISTORY:

GENERAL EXAMINATION:

SENSORIUM:

ANEMIA: JAUNDICE: EDEMA: BMI:

BP: HR: TEMPERATURE: RR:

SYSTEMIC EXAMINATION:

CVS:

RS:

OBSTETRIC EXAMINATION:

Fundal height:

Acting

Presenting part

FHR

PER VAGIAL EXAMINATION:

Bishop score:

ADMISSION CTG:

DIAGNOSIS:

INVESTIGATIONS:

Urine albumin:

Blood grouping & typing: Complete blood count:

Renal function tests: Liver function tests:

Serum uric acid:

TREATMENT:

S. NO.	TIME	SYSTOLIC BLOOD PRESSURE	DIASTOLIC BLOOD PRESSURE	NUMBER OF DOSES OF DRUG GIVEN	HEART RATE	CTG
1.	15 MINUTES					
2.	3O MINUTES					
3.	45 MINUTES					
4.	60 MINUTES					
5.	75					

MINUTES

ADDITIONAL DRUG APPLICATION/ CROSS OVER:

MODE OF DELIVERY/ INDUCTION DELIVERY INTERVAL:

BIRTH WEIGHT OF THE BABY:

ADVERSE EFFECTS:

MATERNAL:

HEADACHE

NAUSEA/ VOMITING

LICHENOID RASH

PALPITATIONS

SHORTNESS OF BREATH

MICTURITION DIFFICULITY

PAIN/ NECROSIS AT INJECTION SITE

VISUAL DISTURBANCES

DIZZINESS

TREMOR

FETAL/ NEONATAL:

FHR ABNORMALITIES:

NEONATAL ADMISSION:

NEONATAL HYPOTENSION

NEONATAL HYPOGLYCEMIA

MASTER CHART

S.NO.	IP.NO.	NAME	AGE	PARITY	GA IN WEEKS	BOOKING	BMI Kg/sq.m	SYS BP in mm Hg	DIAS BP in mm Hg	HR per minute	PROTEINURIA	GROUP	TIME TAKEN IN MINUTES	NO. OF DOSES	SYS BP 15MIN mm Hg	SYS BP 30MIN mm Hg	SYS BP 45 MIN mm Hg	SYS BP 60 MIN mm Hg	SYS BP 75 MIN mm Hg	DIAS BP 15MIN mm Hg	DIAS BP 30MIN mm Hg	DIAS BP 45MIN mm Hg	DIAS BP 60MIN mm Hg	DIAS BP 75MIN mm Hg	CROSS OVER	HR/min 15MIN	HR/min 30MIN	HR/min 45MIN	HR/min 60MIN	HR/min 75MIN	INDUCTION	INDUCTION DEL INTERVAL	MODE OF DELIVERY	WEIGHT OF BABY IN Kg	NICU CARE	NEONATAL OUTCOME	ADR
1	54041	Malathy	27	G2P1L1	34	2	32.4	160	114	100	3	1	30	2	160	150				114	90					100	100				1	10	1	2.2	0	1	2
2	54217	Hemalata	26	primi	32	1	30.8	160	118	88	3	1	45	3	150	140				114	90					88	88	86			1	30	1	2.1	0	1	1
3	54936	Isaiamudu	27	primi	30	2	29	170	120	90	3	2	30	2	160	150				116	90					90	96				1	36	1	2	0	1	0
4	55591	Veramani	21	G2P1L1	36	1	30.5	160	114	92	3	1	45	3	160	150	150			100	100	90				92	90	90			1	6	1	2.5	0	1	0
5	55846	Karpagam	21	primi	32	2	31.5	170	116	98	3	1	45	3	160	160	150			100	90	88				98	96	98			1	36	1	2.3	0	1	2
6	56209	Banupriya	26	primi	24	1	28.1	160	120	90	3	2	30	2	160	140				100	80					90	98				1	30	1	1.8	1	2	2
7	56899	Vasanta	19	G3P2L1	29	1	30.2	160	120	86	1	1	45	3	160	150	150			120	116	98				86	88	88			1	32	1	2	0	1	0
8	63550	Ranjitha	30	primi	36	1	31.6	170	110	80	1	2	30	2	160	158				110	98					80	88				1	6	1	2.5	0	1	0
9	63625	Vinitha	21	G2P1L1	38	1	30.1	168	110	90	1	2	45	3	160	160	150			100	90	90				90	96	98			1	6	1	2.7	0	1	0
10	64404	Barkath	28	G4P3L3	36	1	28.5	180	116	92	3	1	30	2	170	150				100	90					92	90				1	3	1	2.8	0	1	0
11	65049	Ilakiya	29	primi	32	2	32.6	166	116	90	1	1	15	1	150					90						90					1	24	2	2.5	0	1	1
12	109	Anandhi	18	G3P2L2	34	1	33.6	174	118	100	3	2	45	3	160	160	150			118	118	100				100	100	102			1	24	1	2.6	0	1	1
13	234	Rani	22	primi	32	2	30.8	170	110	102	1	2	45	3	160	150	150			110	110	100				102	100	100			1	30	1	2.7	0	1	2
14	375	Gayathri	27	primi	36	2	29.7	160	110	90	2	1	45	3	160	160	150			110	110	100				90	90	90			1	9	2	2.8	0	1	0
15	2996	Arthi	19	G2P1L1	34	1	30.4	166	114	98	1	2	30	2	160	150				110	90					98	98				1	4	1	2.5	0	1	0
16	3124	Malliga	28	primi	24	1	29.8	176	120	96	1	1	45	3	170	170	150			120	116	90				96	96	96			1	30	1	1.5	1	2	0
17	3143	Vasantha	32	primi	28	1	30.9	160	110	90	1	2	30	2	160	150				104	90					90	98				1	32	1	1.6	1	1	0
18	4309	Seshi	26	G2P1L1	36	2	31.5	162	114	88	3	1	30	2	160	150				114	98					88	88				1	5	1	2.4	0	1	0
19	4352	Samanasu	30	primi	38	1	32.6	176	130	86	3	2	30	2	170	140				110	90					86	88	90			1	2	2	3	0	1	0
20	4580	Radhika	23	primi	36	1	29.1	166	120	102	2	1	60	4	160	160	150	150		120	118	110	100			102	100	98	98		1	3	1	2.7	0	1	0
21	4590	Devika	29	G4P3L3	32	1	31.8	162	110	100	1	2	45	3	162	162	150			110	100	90				100	100	98			1	24	1	2.2	0	1	0
22	13488	Devi	28	primi	34	2	33.8	172	110	98	3	2	45	3	160	160	150			110	100	90				98	98	98			1	6	1	2.7	0	1	0
23	13894	Suganya	21	primi	34	1	30.2	180	100	90	1	1	105	7	180	178	178	170	170	100	104	90	90	88	1	90	90	90	88	88	1	8	1	2.5	0	1	1
24	13996	Suguna	29	G3P2L2	30	1	28.5	200	120	88	2	2	90	6	180	180	178	170	170	120	118	118	110	110	1	88	90	98	98	100	1	30	1	2.1	1	1	0
25	14100	Logambal	18	primi	36	2	33.5	166	100	86	1	2	75	5	166	166	160	160	158	100	100	90	90	88		88	88	90	98	98	0	3	2	2.9	0	1	2
26	14122	Podumponu	24	primi	32	2	32.9	160	110	90	1	1	60	4	160	160	150	148		110	110	110	98			90	90	90	80		1	24	2	2.3	0	1	0

27	14141	Selvi	19	G2P1L1	34	2	30.8	170	120	80	3	2	45	3	170	168	150			120	128	100				80	90	100			1	24	1	2.6	0	1	0
28	14261	Indrani	25	G2P1L1	38	1	28.9	170	110	78	3	2	75	5	170	168	160	160	150	110	110	110	110	100		78	80	88	88	90	1	4	1	2.8	0	1	0
29	14266	Chithra	30	primi	38	1	30.9	160	110	70	1	1	45	3	160	160	148			110	110	90				70	70	80			1	6	1	3	0	1	1
30	14339	Prema	24	G4P3L3	30	2	34.1	164	110	88	1	2	60	4	164	160	150	150		110	110	108	90			88	88	98	98		1	36	1	2.3	0	1	0
31	14495	Mariammal	29	primi	34	2	33.1	172	110	80	3	2	60	4	160	160	160	140		110	108	100	90			80	90	90	98		1	6	1	2.2	0	1	2
32	14702	Kavitha	28	G3P2L1	32	2	29.1	178	104	78	1	2	45	3	170	160	150			100	90	90				78	80	90			1	12	1	2.1	0	1	2
33	15418	Eswari	20	primi	36	1	32.4	170	110	76	2	2	30	2	160	150				100	90					76	80				1	8	1	2.8	0	1	1
34	15449	Nazeema	31	G2P1L1	34	1	33.9	168	112	74	2	1	45	3	160	158	140			112	100	90				74	74	74			1	10	1	3	0	1	0
35	15663	Kavitha	31	primi	36	1	30.7	164	100	78	3	2	30	2	160	140				90	88					80	90				1	7	2	2.8	0	1	0
36	16231	Firdose	24	primi	30	2	32.1	160	110	80	2	1	45	3	160	160	150			100	90	80				80	80	78			1	24	2	2.4	0	1	0
37	16421	Palaniamal	30	G2P1L1	36	2	32.3	160	120	90	3	2	30	2	160	140				110	90					90	100				0	8	1	2.8	0	1	3
38	20642	Radhika	34	primi	38	1	34.3	170	120	100	3	1	45	3	170	168	150			110	100	90				100	98	90			1	4	2	3	0	1	0
39	20869	Jeya	29	primi	34	1	35.1	168	122	98	2	2	45	3	150	150	140			120	110	98				98	98	98			1	4	2	2.8	0	1	0
40	20943	Vinodha	31	primi	34	1	31.7	172	100	90	3	1	45	3	170	158	140			90	90	80				90	90	88			1	8	2	2.8	0	1	1
41	21193	Jamuna	28	G3P2L2	32	1	29.7	170	110	80	2	2	60	4	170	160	160	150		110	110	110	90			80	88	98			1	24	1	2.3	0	1	2
42	21432	Sajinisha	23	G3P2L1	30	2	29.1	180	110	78	3	1	60	4	180	176	160	148		100	98	90	90			78	78	80	78		1	30	1	2	0	1	2
43	21723	Mersiyal	20	primi	36	2	30.5	180	114	90	3	1	75	5	180	170	170	150		114	100	90	90			90	90	88	80	80	1	6	1	2	0	1	0
44	21859	Suseela	23	G3P2L0	28	1	34.1	178	120	80	3	1	60	4	170	168	160	140		110	100	90	90			80	80	80	80		1	32	1	1.6	1	1	0
45	21888	Ramya	27	primi	34	1	29.8	160	110	76	2	2	30	2	160	148				100	90					78	80				1	6	2	2	0	1	0
46	21892	Vijaya	33	primi	36	1	25.8	180	112	86	2	1	45	3	180	180	150			112	110	98				86	80	80			1	7	2	2.5	0	1	1
47	21918	Mani	20	primi	34	1	29.4	166	114	98	2	1	30	2	160	150				110	90					98	90				1	6	2	2	0	1	0
48	22197	Danam	27	G2P1L1	33	2	30.4	176	100	90	2	2	30	2	170	148				90	88					90	100				1	28	1	2	0	1	0
49	23750	Satya	29	primi	28	1	33.1	178	110	100	1	1	15	1	150					90						100					1	30	1	1.8	1	1	6
50	23928	Tamarai	29	G2P1L1	24	1	29.6	170	112	88	1	2	45	3	160	148	140			112	110	90				88	90	90			1	36	1	1	1	2	0
51	24233	Ammu	18	primi	32	1	28.2	160	116	90	1	2	45	3	160	158	140			100	90	88				90	90	96			1	24	2	2	1	1	0
52	24261	Chellaya	29	primi	34	1	35.3	200	118	98	3	1	105	7	200	180	180	178	170	118	110	100	100	100	1	98	90	90	88	88	1	7	1	2.1	0	1	0
53	24801	Rajeswari	20	G3P1L1A1	38	1	29.5	160	120	90	1	2	60	4	160	158	150	140		120	118	110	100			90	98	98	98		1	4	1	3	0	1	0
54	24853	Sundarambal	19	primi	32	1	28.6	166	110	90	2	1	45	3	160	158	140			110	90	88				90	90	90			1	6	1	2.8	0	1	0
55	24856	Mumtaj	24	G4P1L1A2	34	2	26.4	160	114	90	2	2	75	3	160	150	148			110	100	90				90	92	100			1	3	1	2	0	1	0
56	24981	Vimala	30	G2P1L1	28	1	29.1	170	118	90	3	1	90	6	170	170	170	168	160	118	110	110	110	100	1	90	90	80	80	80	1	24	1	2.5	0	1	6
57	25292	Prabavati	22	primi	26	1	28.5	178	120	92	3	2	75	5	170	170	168	160	150	110	100	100	90	90		92	90	94	98	100	1	20	1	1.2	1	2	0
58	25385	Sheelamary	21	primi	32	2	30.5	176	110	94	3	1	75	5	170	160	158	150	140	110	100	100	90	88		94	90	90	88	88	1	6	2	2.1	0	1	0
59	25412	Amsavalli	26	primi	32	2	27.5	180	106	98	1	1	60	4	180	178	170	160		106	100	90	88			98	90	88	88		1	8	2	2	0	1	0
60	25847	Malathy	25	primi	26	1	32.5	180	118	90	1	2	90	6	180	178	170	170	160	110	110	110	110	100	1	90	94	98	98	100	1	30	2	1	1	2	0
61	26056	Panjavarnam	28	primi	30	1	32.4	170	110	70	1	1	75	5	170	170	168	160	150	110	110	108	100	90		70	70	72	70	70	1	9	1	2	0	1	0
62	26272	Yogarani	26	G2P1L1	26	1	29.7	170	120	74	2	2	75	5	170	160	160	158	150	120	110	110	108	90		84	88	90	90	90	1	26	1	1.2	1	2	0
63	26457	Sangaatha	30	G2P1L1	28	1	32.5	170	116	70	1	1	60	4	168	160	150	140		110	110	106	98			70	72	70	70		1	30	1	1	1	2	0
64	26521	Kalaivani	31	primi	32	2	28.5	166	116	78	2	1	45	3	150	150	148			116	110	100				78	80	80			0	10	1	2	0	1	0
65	26610	Jenitha	22	primi	34	2	27.9	176	110	70	2	2	15	1	150					100						70					1	9	1	2.2	0	1	0
66	26730	Periyakke	26	primi	36	1	29.1	160	110	88	1	1	105	7	160	160	160	158	150	110	110	110	110	110	1	88	88	90	88	90	1	8	1	2.6	0	1	0
67	26790	Jeeva	28	primi	34	1	27.2	160	110	80	3	2	75	5	160	158	156	150	140	110	110	106	106	98		80	82	88	90	90	1	6	2	2.4	0	1	0
68	26908	Pongodi	21	G4P2L1A1	32	1	33	160	120	70	3	1	75	5	160	160	158	150	140	120	118	100	98	88		70	70	68	70	72	0	6	1	2.1	0	1	0
69	27052	Chithra	27	primi	34	1	33.8	166	100	74	1	2	30	2	150	140				100	90					74	80				1	8	1	2.1	0	1	0

70	27123	Vijaya	22	G3P1L1A1	32	2	32.9	172	100	70	1	2	105	7	172	170	170	170	160	100	98	90	90	90	1	72	78	88	88	90	1	8	1	2.2	0	1	0
71	27142	Vasantha	20	primi	28	1	34.5	170	106	70	1	1	60	4	170	170	160	150		100	90	90	90			70	70	70	68	70	1	30	1	1.5	1	2	0
72	27413	Geetha	19	G2P1L1	36	1	32.1	166	120	80	2	1	60	4	166	160	150	140		110	110	108	80			80	80	86	86		1	5	1	2	0	1	0
73	27463	Nadhiya	20	primi	30	1	33.1	164	120	88	1	1	45	4	164	160	160	140		120	110	110	100			88	80	80	80		0	3	2	2	0	1	0
74	27531	Logambal	19	G2P1L1	34	2	32.5	160	112	80	3	2	75	3	160	140	130			112	110	90				82	88	90			1	5	1	2.1	0	1	0
75	27574	Manimegalai	28	primi	36	2	29.4	170	100	80	1	1	15	1	150					90						82					1	6	2	2.5	0	1	0
76	27596	Rajeshwari	20	primi	38	2	29.9	170	102	90	1	2	60	4	160	158	158	150		102	100	100	90			92	98	98	100		0	3	2	3	0	1	3
77	27798	Banumathy	29	primi	36	2	28.5	170	110	90	1	1	45	3	170	160	150			110	100	90				90	90	88			1	5	1	2.5	0	1	0
78	28127	Saradha	23	G4P3L3	32	2	30.5	172	100	100	2	1	60	4	172	170	150			100	98	88				100	100	98	90		0	2	1	2.5	0	1	0
79	28376	Anusha	26	primi	34	2	31.6	166	110	106	3	1	75	5	166	160	140			100	90	90				104	100	90	90	90	1	5	1	2	0	1	0
80	28523	Jansirani	28	G3P1L1A1	36	2	32.5	168	120	88	3	2	30	2	160	140				110	98					88	80				1	4	1	2	0	1	1
81	28646	Chandra	24	primi	32	1	29.8	160	114	90	1	1	75	5	160	158	150	140		114	110	110	100			90	90	88	90	90	1	3	2	2.1	0	1	0
82	28710	Maheswari	29	G4P1L1A2	34	2	30.4	170	120	98	1	2	60	4	170	160	160	148		110	110	108	90			98	98	96	98		1	1	2	1.8	1	1	0
83	28783	Usha	30	primi	30	2	32.6	170	100	72	2	2	30	2	160	148				100	90					72	80				1	2	2	2.1	0	1	1
84	28996	Mani	21	primi	38	2	31.5	172	100	80	2	1	45	3	170	168	150			100	90	88				80	80	80			1	3	2	3	0	1	4
85	29184	Rajathi	19	G2P1L1	36	2	29.4	174	100	68	3	2	105	7	174	170	160	160	160	100	100	100	100	100	1	70	80	88	98	98	1	5	1	3	0	1	4
86	29327	Revathy	20	primi	38	2	28.9	170	110	70	3	2	60	4	168	160	150	150		110	108	108	98			78	88	88	90		1	3	2	3.1	0	1	4
87	30730	Amudha	30	primi	28	1	33.9	180	104	64	1	2	60	4	178	170	168	146		100	98	90	88			70	78	90	90		1	30	1	1.6	1	2	4
88	30939	Vanitha	30	primi	30	1	38.1	182	100	68	1	1	90	5	182	180	170	150		100	100	98	90			68	70	70	72	72	1	6	1	2	0	1	5
89	31411	Shameem	22	primi	30	1	32.5	180	100	70	1	2	30	2	170	150				100	80					70	78				1	6	2	2.1	0	1	0
90	31623	Ranjitha	27	primi	28	1	27.1	180	102	74	1	1	30	2	180	150				90	80					76	70				1	24	2	1.8	1	2	0
91	31774	Priya	26	G3P2L2	30	2	26.7	184	104	80	3	2	30	2	170	148				90	80					88	88				1	20	1	2.5	0	1	4
92	31929	Jeenath	25	primi	32	2	29.7	180	120	88	3	1	30	2	140					100	90					88	86				1	30	1	2	0	1	0
93	32119	Rinku	24	primi	36	2	33.2	166	104	90	2	1	45	3	160	158	130			90	90	80				90	90	88			0	2	2	2.3	0	1	5
94	32321	Sheela	24	primi	28	1	35.6	170	100	94	2	2	30	2	160	140				100	80					94	94				1	24	1	1.4	1	2	0
95	32336	Shobana	21	primi	30	2	31.3	172	104	80	1	2	45	3	168	160	140			100	90	88				80	88	90			1	7	1	2	0	1	1
96	49140	Meena	30	G2P1L1	32	1	28.2	170	104	70	1	2	45	3	170	168	150			100	90	80				78	80	90			1	6	1	2.2	0	1	0
97	49205	Sofia	18	primi	28	1	28.9	170	100	64	2	1	15	1	150					90						68					1	24	1	1.2	1	1	4
98	49241	Jothi	20	G3P1L1A1	30	1	30.5	166	112	68	2	2	30	2	150	140				110	90					70	80				1	8	1	2	0	1	4
99	49396	Lalitha	19	primi	34	2	32.7	180	120	70	2	2	105	7	180	180	170	168	160	120	120	120	118	110	1	70	78	80	80	86	1	5	2	2	0	1	4
100	49538	Nadhiya	21	primi	36	2	31.5	200	122	70	1	1	45	3	180	160	150			118	110	100				70	70	72			1	5	2	2.2	0	1	0
101	50035	Geetha	24	G2P1L1	30	2	32.4	178	120	80	1	2	105	7	178	176	170	168	160	120	120	120	110	110	1	80	80	84	90	98	1	7	1	2	0	1	3
102	52110	Hema	18	primi	30	2	32.6	188	114	88	1	1	90	6	188	180	180	170	170	110	110	110	100	100	1	88	80	80	78	80	1	8	1	2	0	1	0
103	52454	Buvaneswari	20	primi	34	1	28.9	180	100	90	1	1	45	3	170	158	150			90	90	80				90	90	80			1	10	1	2.5	0	1	0
104	52730	Vasantha	24	primi	38	2	30.5	170	100	80	3	1	60	4	170	170	160	150		100	90	90	90			80	80	82	78		0	8	1	3	0	1	0
105	52988	Annakamu	23	primi	36	2	26.7	168	114	88	3	1	30	2	160	150				100	90					88	88				1	8	2	2.5	0	1	4
106	53401	Rosemary	25	G2P1L1	38	2	30.5	172	118	80	1	2	60	4	160	158	150			118	110	100	90			80	82	88	90		1	5	1	3	0	1	3

ABBREVIATIONS

BOOKING

1	Booked
2	Unbooked

GROUP

1	Labetalol
2	Nifedipine

GA	Gestational Age
BMI	Body Mass Index
SYS BP	Systolic Blood Pressure
DIAS BP	Diastolic Blood Pressure
HR	Heart Rate

INDUCTION

0	Induction with cerviprime gel
1	No induction

MODE OF DELIVERY

1	Labour natural
2	Caesarean section

NICU (NEONATAL INTENSIVE CARE UNIT) ADMISSION

0	Not admitted
1	Admitted in NICU

NEONATAL OUTCOME

1.	Alive
2.	Dead

ADR (ADVERSE DRUG REACTIONS)

0	No notable adverse effects
1	Dizziness
2	Headache
3	Palpitations
4	Nausea

5	Tremor
6	Pain at the injection site
7	Wheezing
IUGR	intrauterine growth restriction
sFLT	soluble fms- like tyrosine kinase
VEGF	vascular endothelial growth factor
PDGF	platelet derived growth factor
PGI_2	prostaglandin I_2
PGE_2	prostaglandin E_2
KIR	killer cell immunoglobulin like receptor
HLA	human leukocyte antigen
NK cells	natural killer cells
MRI	magnetic resonance imaging
HELLP	hemolysis, elevated liver enzymes, low platelet count